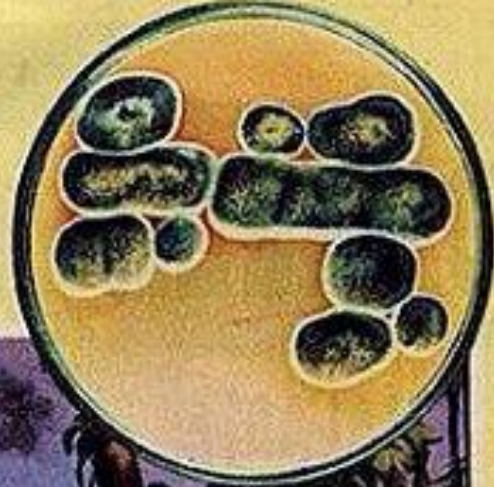


抗生素使用與管理作為對於抗 藥性細菌發展的重要性

高醫附設醫院 感染內科

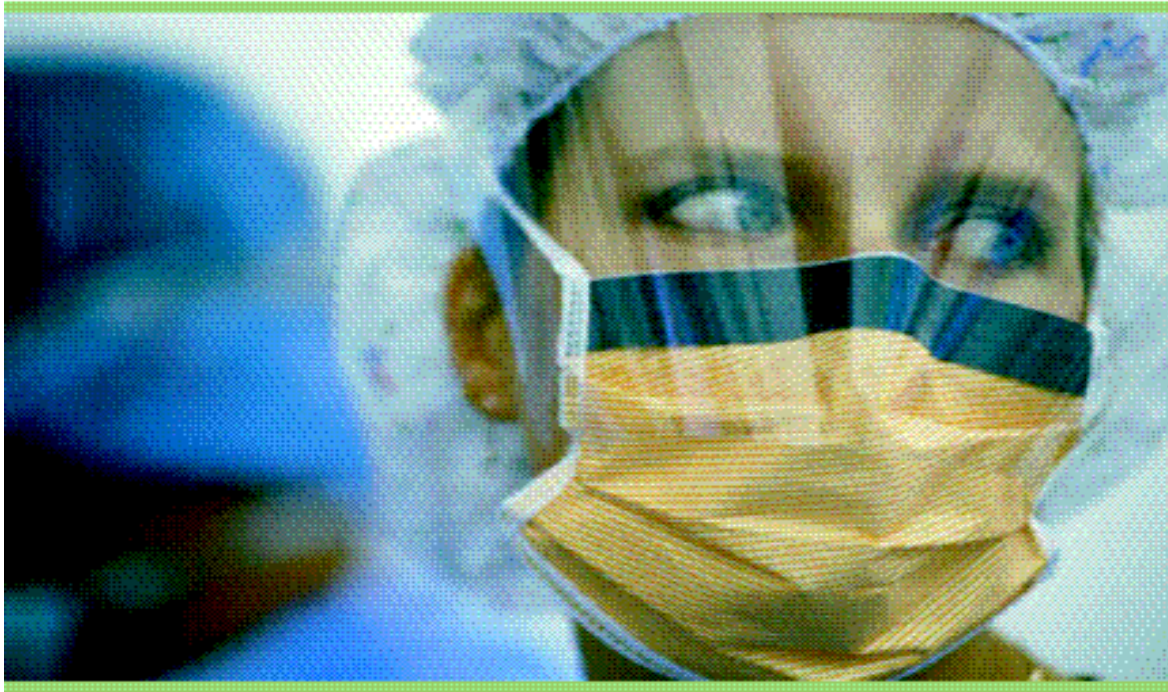
盧柏樑 醫師

Thanks to PENICILLIN
...He Will Come Home!



BAD BUGS, NO DRUGS

As Antibiotic Discovery Stagnates ...
A Public Health Crisis Brews



July 2004

Bad Bugs, No Drugs¹

1. Infectious Diseases Society of America. Bad Bugs, No Drugs: As Antibiotic Discovery Stagnates, A Public Health Crisis Brews. http://www.idsociety.org/pa/IDSA_Paper4_final_web.pdf. July, 2004. Accessed March 17, 2007. 2. Talbot GH, et al. *Clin Infect Dis*. 2006;42:657-68.

Contents

- 感染症之治療
- 抗藥性的影響
- 為什麼會產生細菌抗藥性?
- 辨別培養出的細菌是否為真的致病菌?
- 細菌抗藥性之流行病學
- 面對抗藥性

感染症之治療

- Antimicrobial agents
 - Antibiotics
 - Synthetic antimicrobial agents
- Immunization
- 針對會在單位內傳播中感染症 → Infection control

Antimicrobial agents

- Paul Ehrlich: 606 for syphilis. 1908 Nobel prize
- Gerhard Domagk: KL730 Sulfa drug for Streptococcus
- Flemming: Penicillin



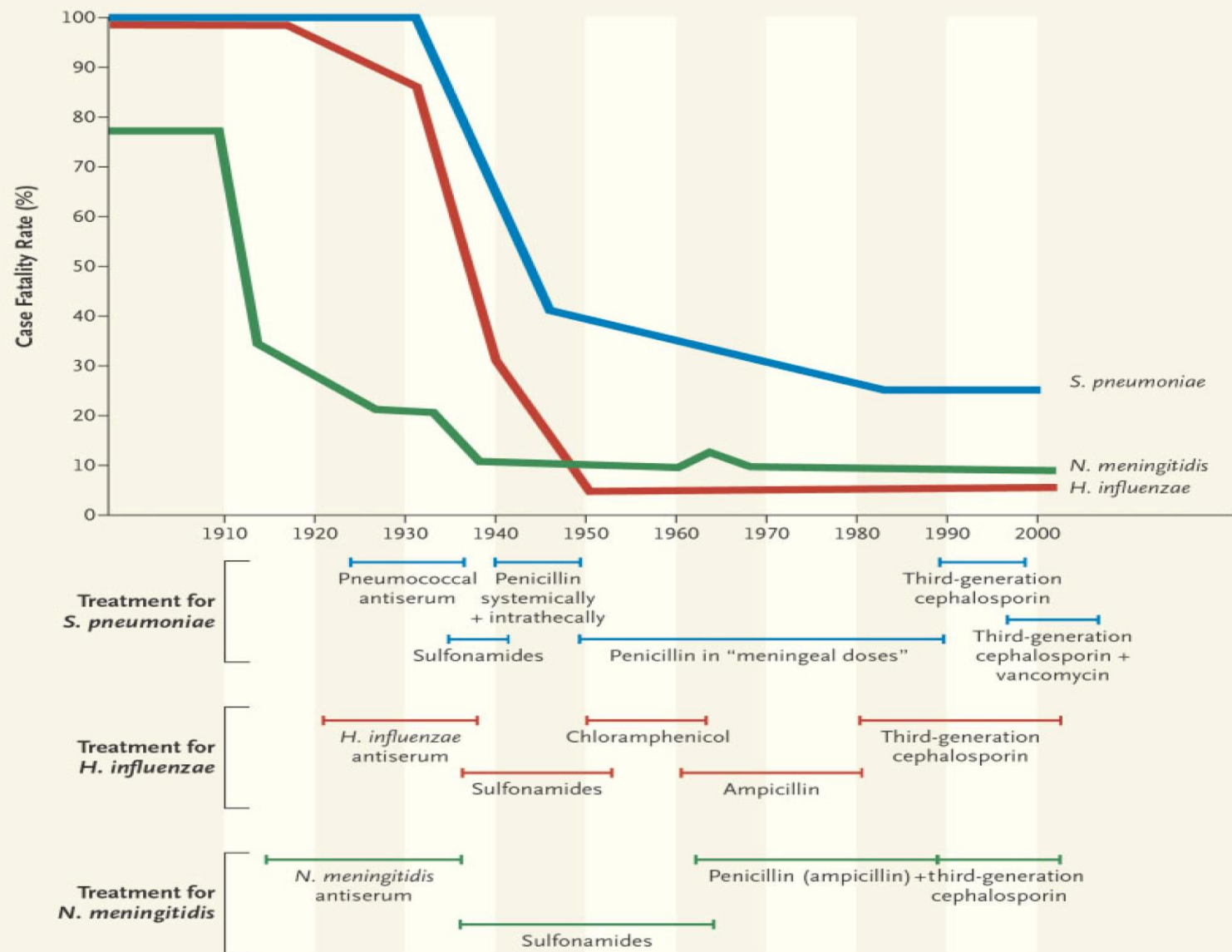
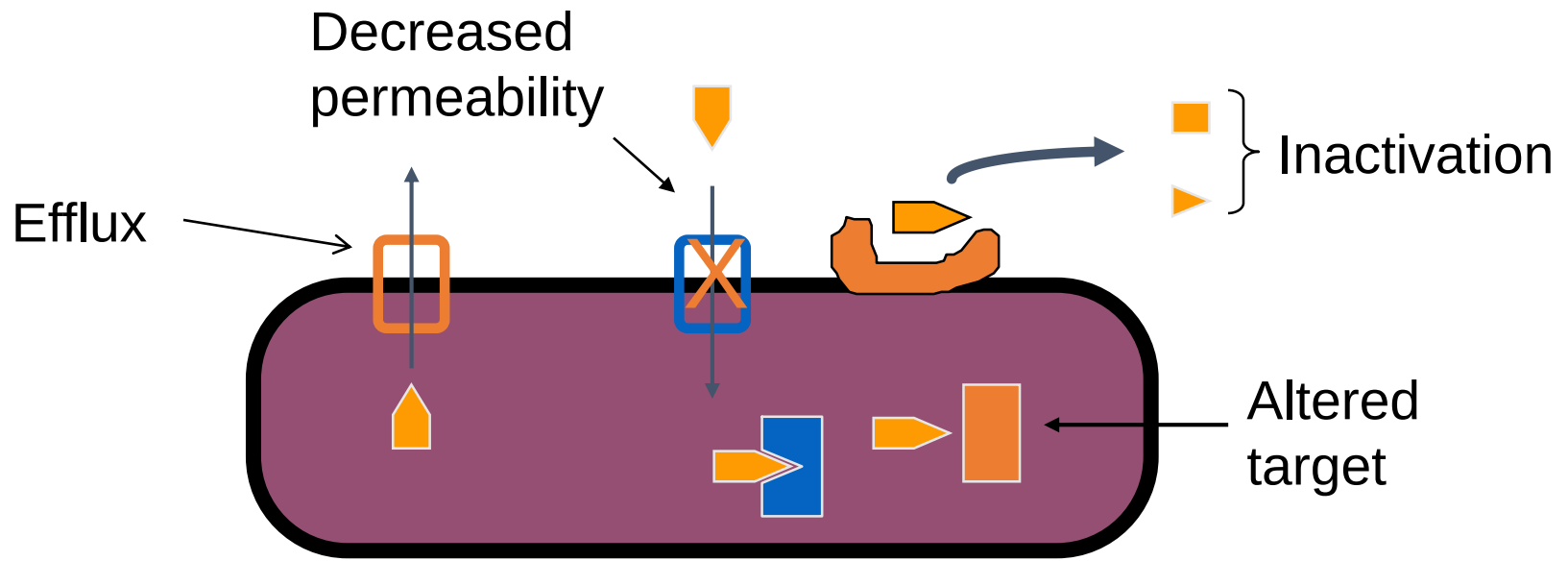


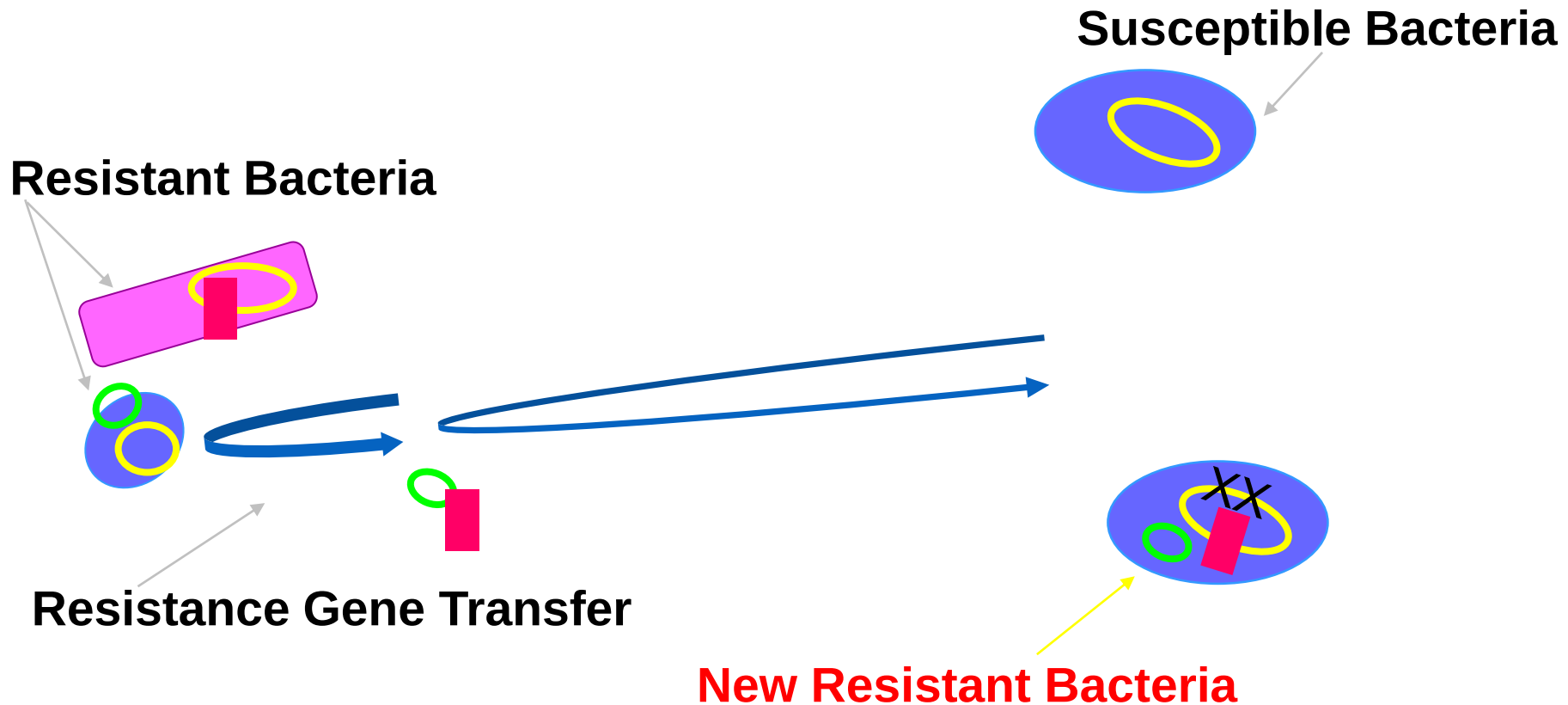
Figure. Mortality Rates Associated with Community-Acquired Bacterial Meningitis over the Past 90 Years.

Mechanisms of Resistance

- Antibiotics exert selective pressure that favors emergence of resistant organisms
- Bacteria employ several biochemical strategies to become resistant



Emergence of Antimicrobial Resistance

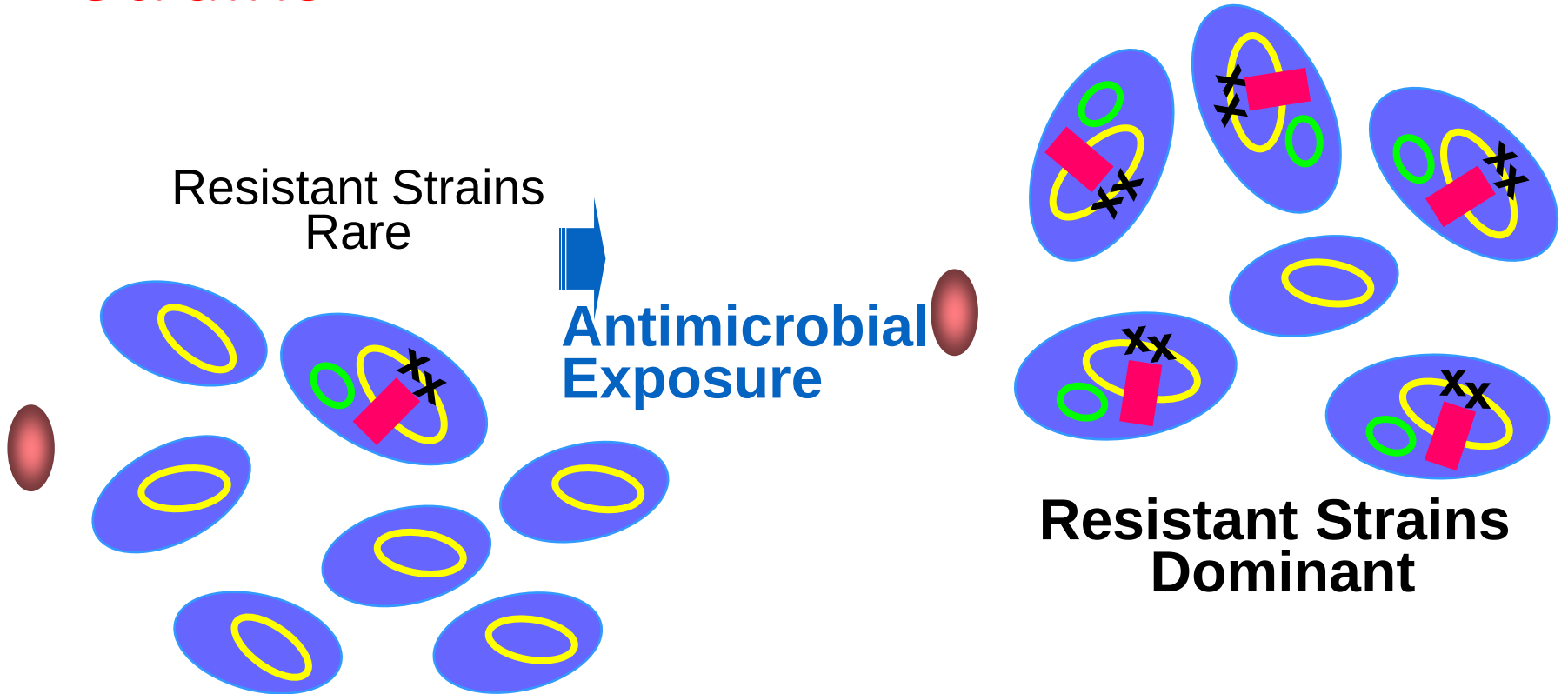


Selection for antimicrobial-resistant Strains

Resistant Strains
Rare

Antimicrobial
Exposure

Resistant Strains
Dominant

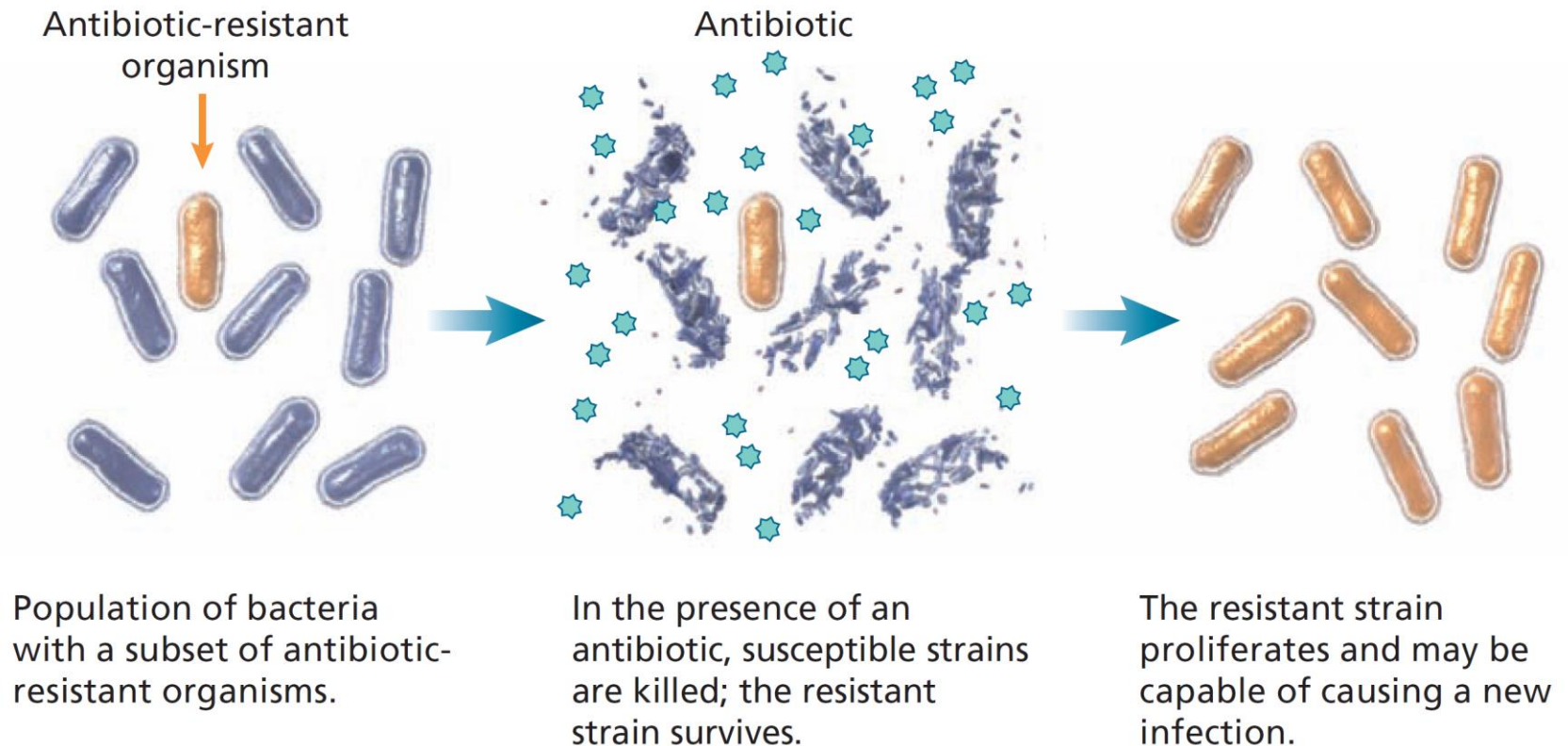


為什麼抗藥性菌種增加？

對策？

- Antimicrobial use
 - Selection pressure
- patient-to-patient transmission of resistant strains
 - Transmission

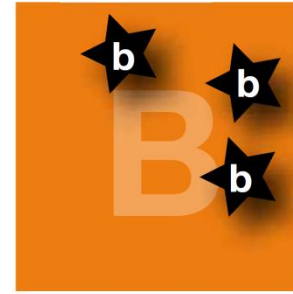
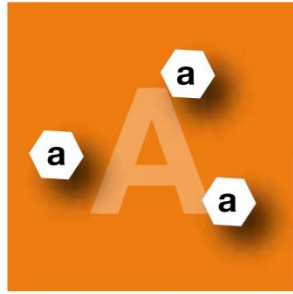
Selection for antimicrobial-resistant Strains



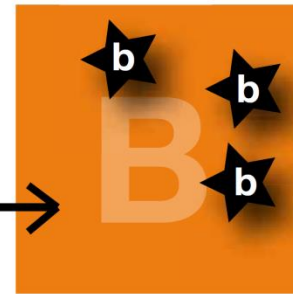
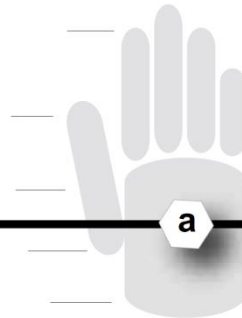
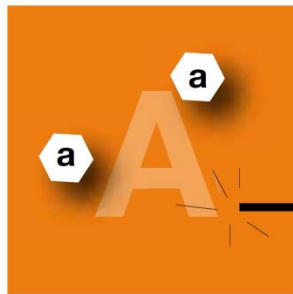
死掉的細菌不會產生抗藥性

What does not kill me makes me stronger.

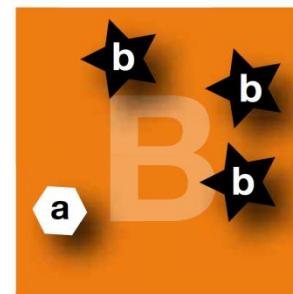
1



2



3



細菌的傳播



Feinbo



抗生素使用與管理作為

- 有沒有醫師不希望可以自由的開藥？
- 為何感染科醫師可以為醫院管理抗生素？

Evolution and dissemination of MRSA

Discovery of

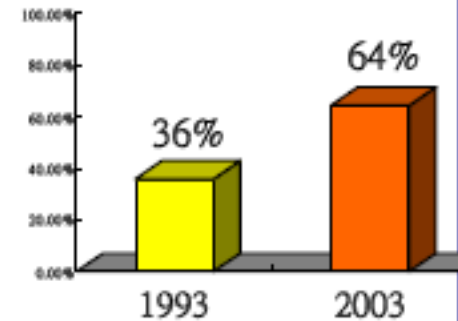
Staphylococcus aureus



1940s
Penicillin

1959
Methicillin

MRSA



1880

1950s-1960s

1961

1970's

1980s

1992-2003

Penicillin-resistant
Staphylococcus aureus
dissemination in the
community

Outbreaks of MRSA

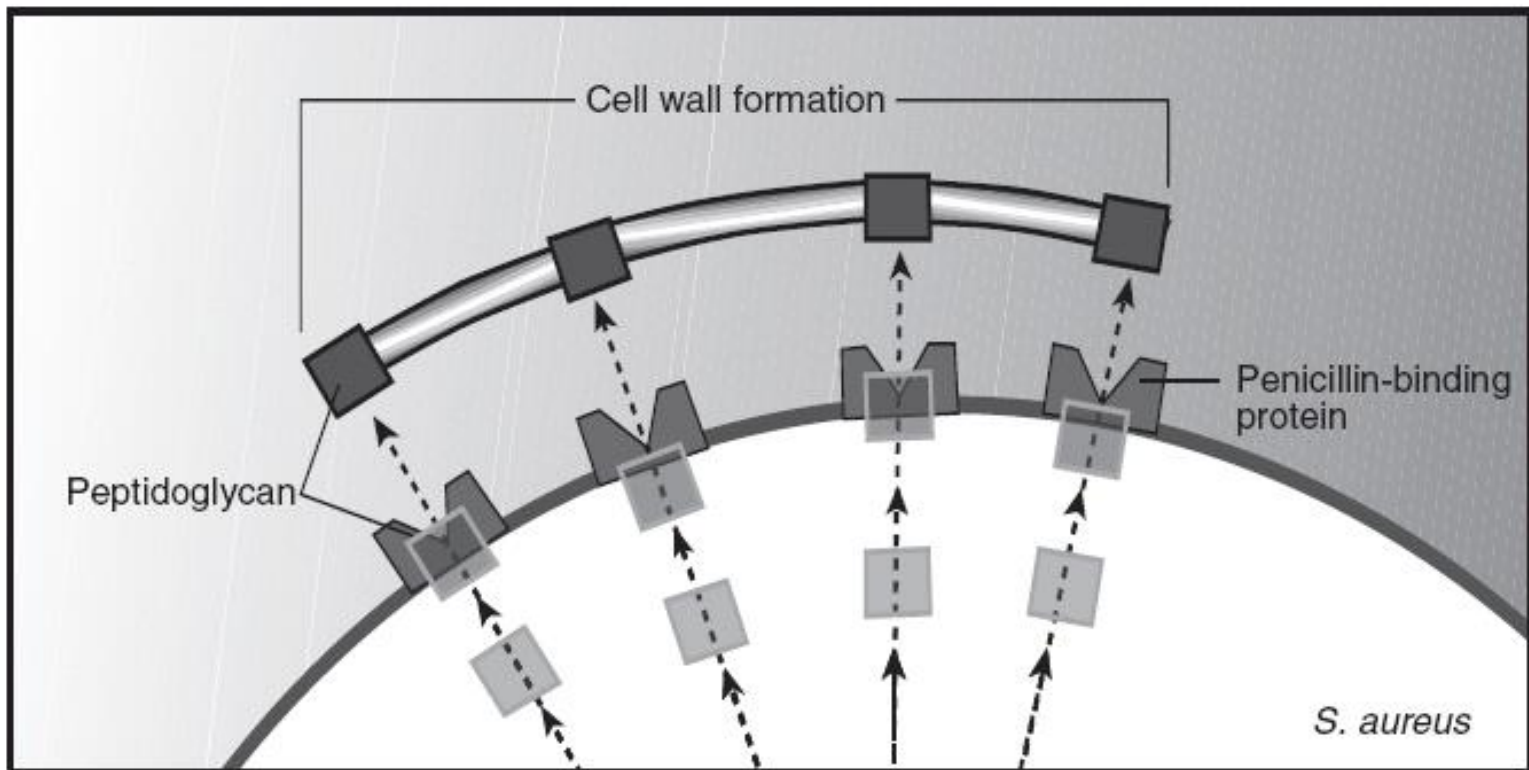
Endemic in hospitals

MSSA: oxacillin, cefazolin
MRSA: vancomycin,.....

Klevens, et al Clin Infect Dis 2006;42;389-91

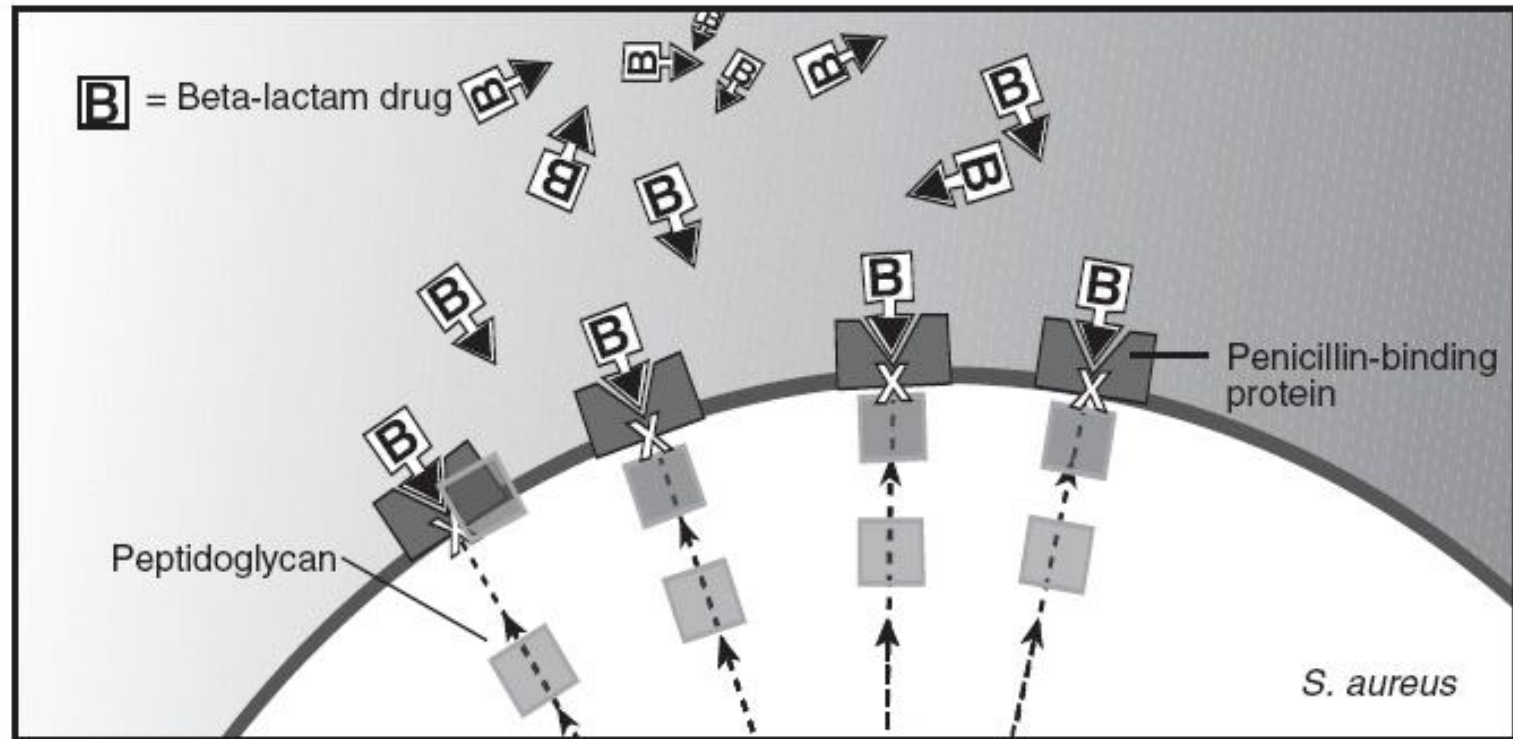
Mechanism of methicillin resistance -1

Penicillin-binding proteins cross-link peptidoglycan, facilitating *S. aureus* cell wall formation and cell growth.



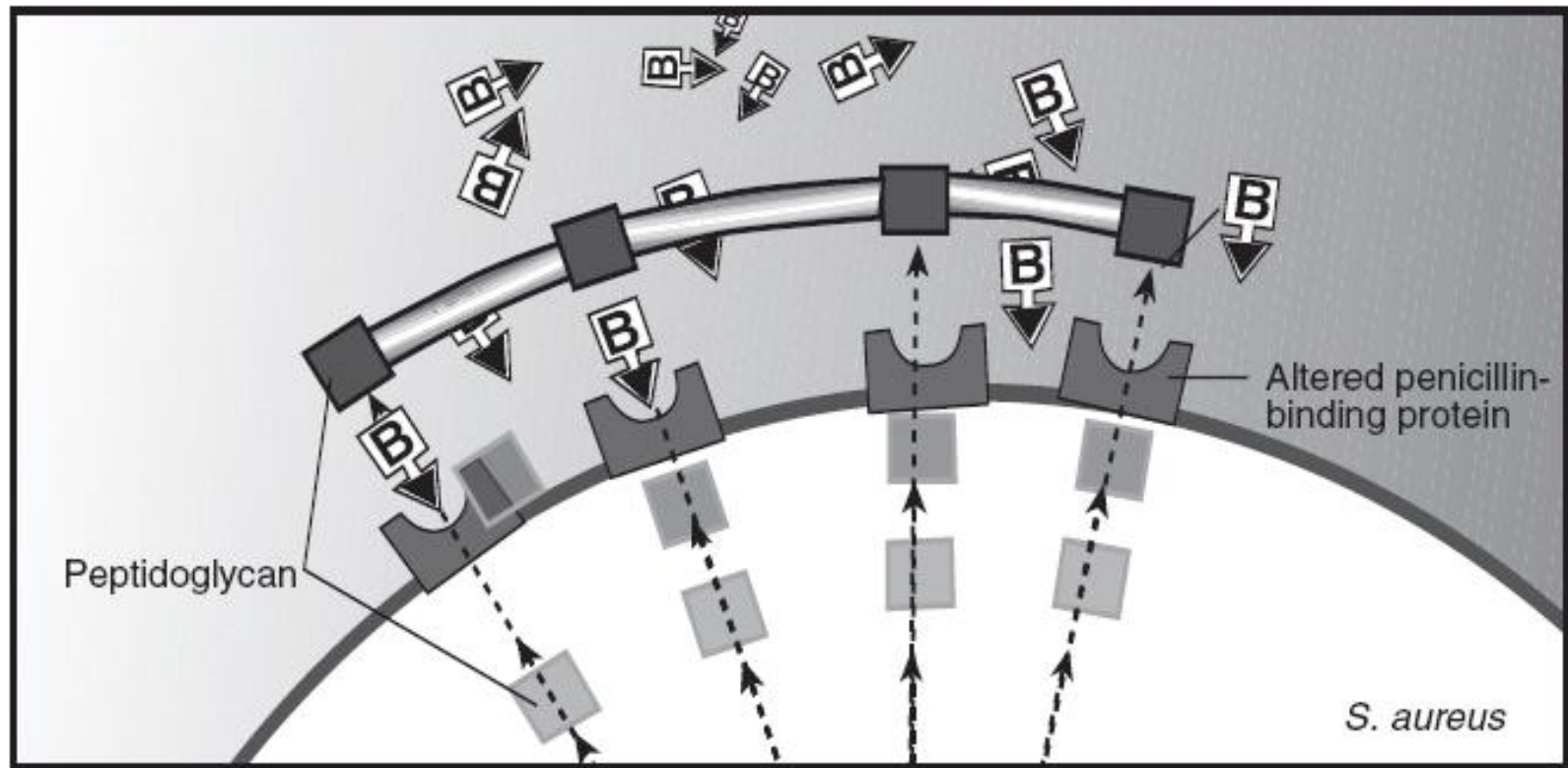
Mechanism of methicillin resistance -2

Beta-lactam drugs (such as penicillin and methicillin) bind to penicillin-binding proteins, blocking the cross-linking of peptidoglycan. Since the *S. aureus* cell can no longer form an adequate cell wall, growth is inhibited.



Mechanism of methicillin resistance -3

Methicillin-resistant *S. aureus* cell has altered penicillin-binding proteins, to which beta-lactam drug cannot bind, allowing continued cell wall formation.

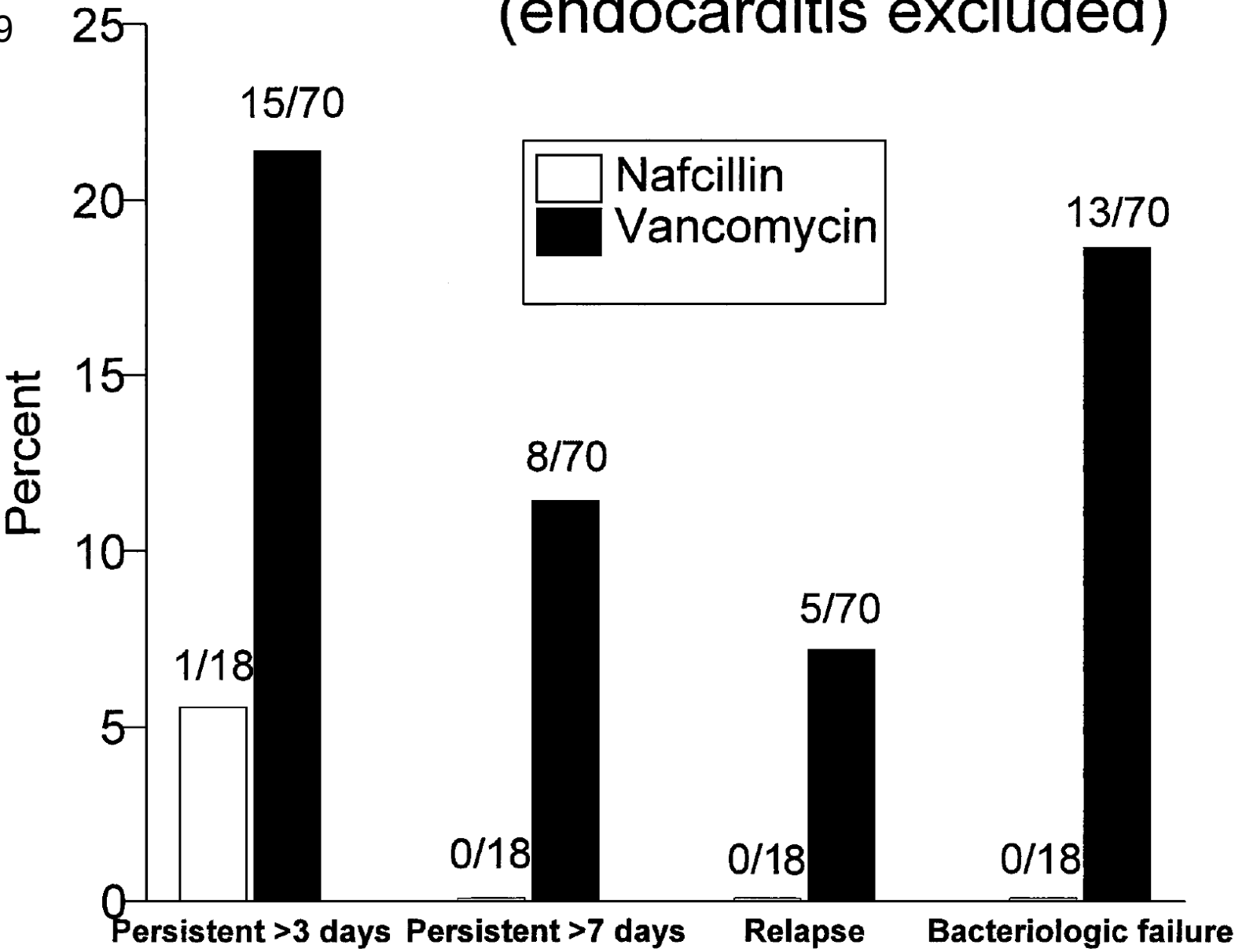


MRSA is resistant to all current PCNs, cephalosporins and carbapenems

MSSA Tx options

- cefazolin
- Oxacillin
-
- Vancomycin (X)

MSSA Bacteremia (endocarditis excluded)



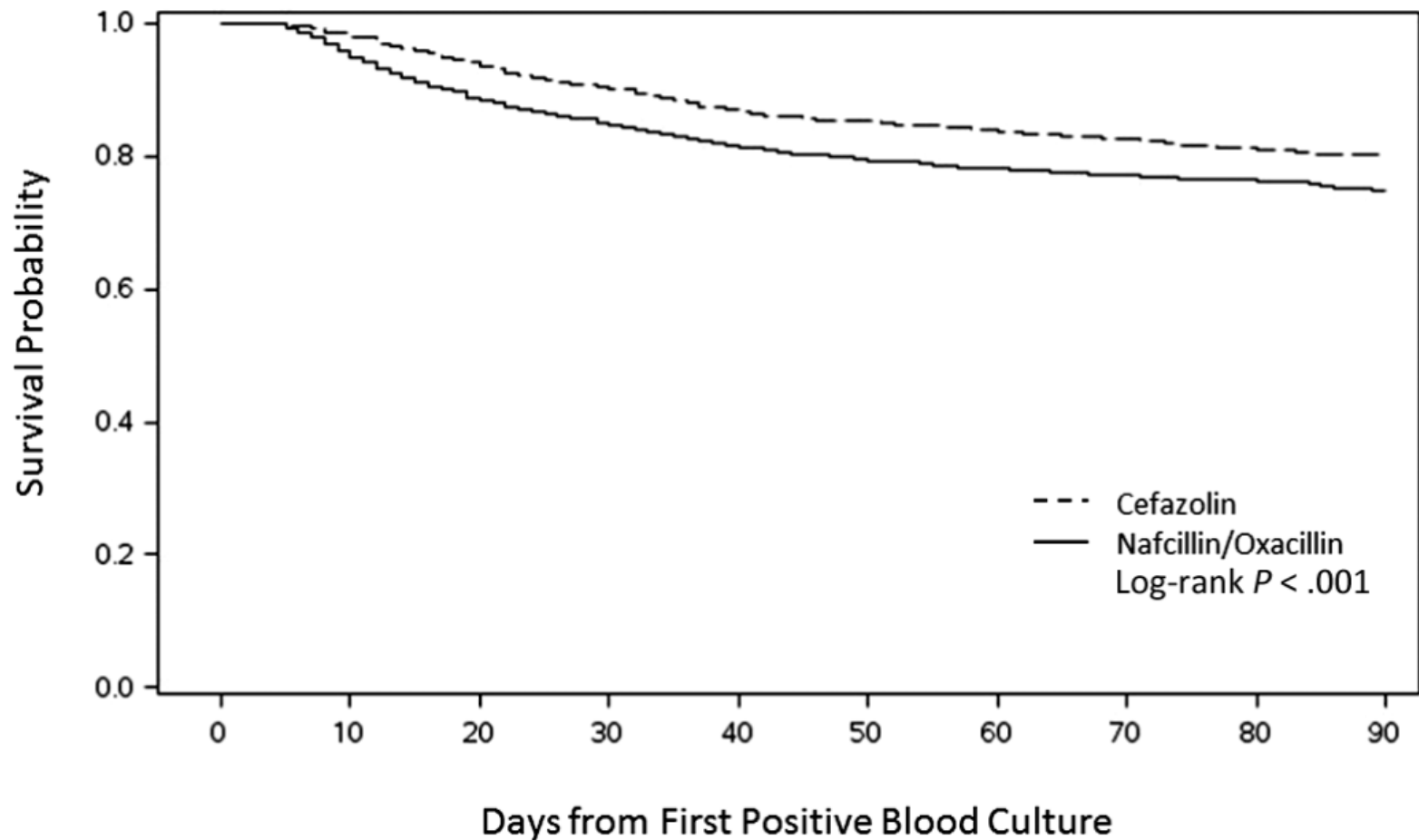


Figure 2. Kaplan–Meier curve of mortality comparing patients who received cefazolin vs patients who received nafcillin or oxacillin for methicillin-susceptible *Staphylococcus aureus* infections complicated by bacteremia.

抗生素使用與管理作為

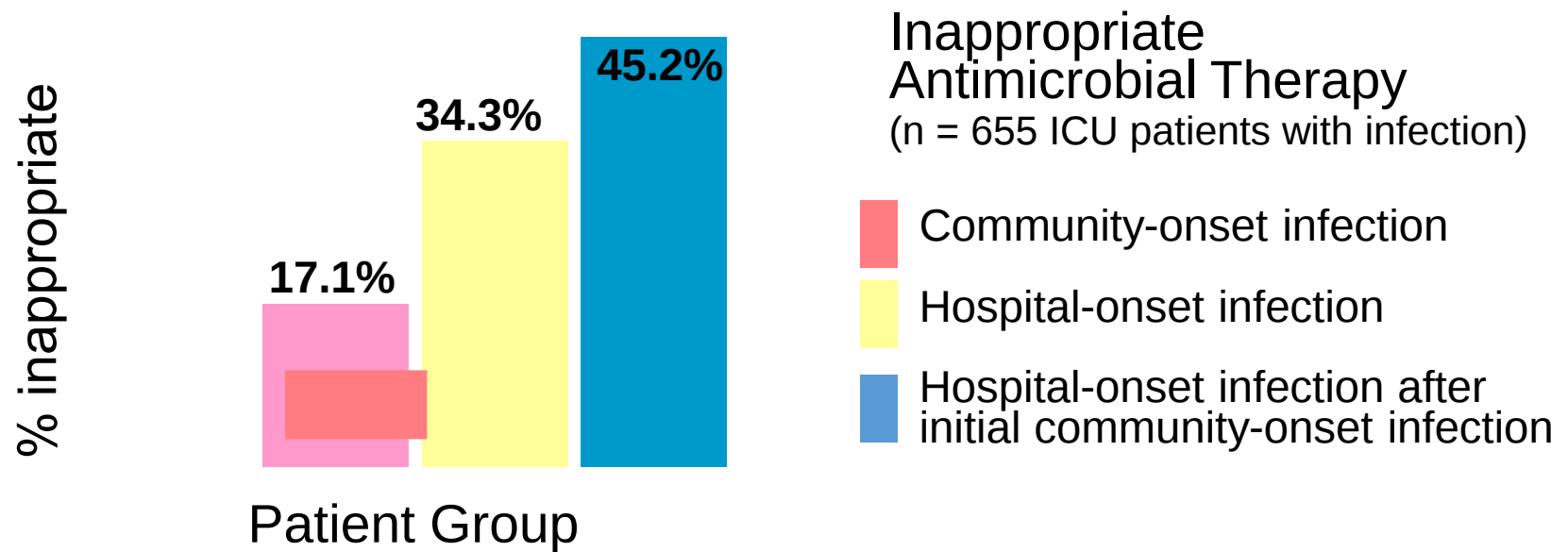
- 有沒有醫師不希望可以自由的開藥？
- 為何感染科醫師可以為醫院管理抗生素？

不是使用貴的抗生素就是對病人好
不是使用後線抗生素就是對感染病人最好的選擇

適當使用為佳



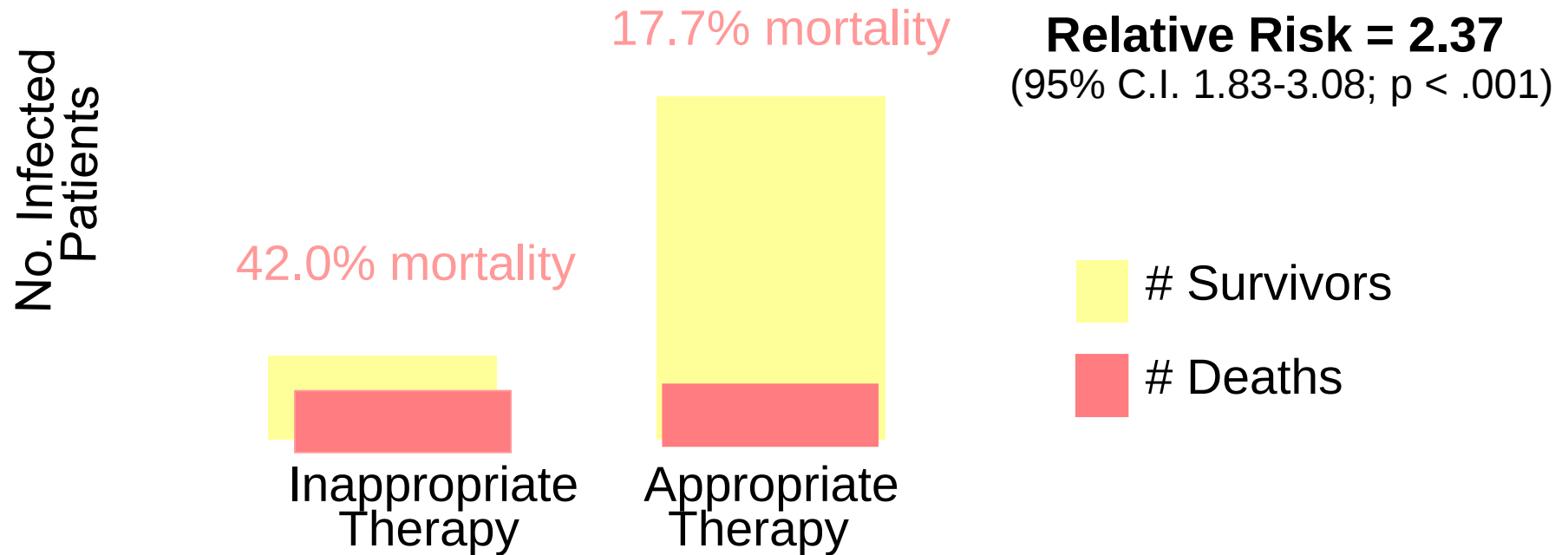
Inappropriate Antimicrobial Therapy: Prevalence among Intensive Care Patients



Source: Kollef M, et al: *Chest* 1999;115:462-74



Inappropriate Antimicrobial Therapy: Impact on Mortality



Source: Kollef M, et al: Chest 1999;115:462-74

Risk factors of ciprofloxacin resistance in urinary *Escherichia coli* isolates.

- urinary catheterization
- prior quinolone exposure

Lin CY, et al. J Microbiol Immunol Infect. 2008 Aug;41(4):325-31.

True Pathogen? Colonization?

細菌室報告

檢體名稱：

Sputum (urine ; wound swab)

報告：

1. *Serratia marcescens* (3+)
2. Viridans streptococcus (3+)
3. Neisseria species (3+)

AM: Ampicillin	R
AMC: Amoxi./Clavu	R
CZ: Cefazolin	R
CMZ: Cefmetazole	R
CTX: Cefotaxime	R
GM: Gentamicin 10µg	R
AN: Amikacin	S
IPM: Imipenem	S
CIP: Ciprofloxacin	R
FEP: Cefepime	R
AZM: Aztreonam	R

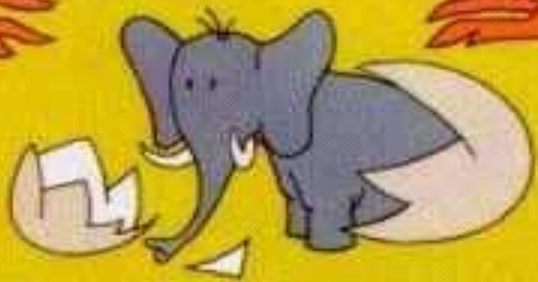
1.

常見的污染菌

- Coagulase-negative staphylococci
- Staphylococcus epidermidis
- Viridans streptococci
- Micrococci
- Bacillus species
- Corynebacterium species
- Neisseria species (除N. gono及meningitidis)
- Nonfermentative gram-negative bacilli
 - Acaligenes, Flavobacterium, Sphingomonas...

這是真的嗎？

BARAK



先確定病原是否有意義

血液或無菌體液培養(腦脊髓液，肋膜積水..).

痰液培養：

- 聽診有囉音或敲診有濁音
- 新發生的膿痰或是痰液的顏色改變。
- 血液培養陽性或由bronchial washing或biopsy培養出菌。
- 肺部X光有新增或惡化的浸潤，開洞或肋膜積水。

泌尿道培養：

- 泌尿道症狀及尿液培養有大於 10^5 菌落/ml。
- 培養出的微生物需小於三種。
- 泌尿道症狀加上WBC esterase或nitrate陽性，或膿尿(>10 WBC/HPF)或重複培養出同一之細菌 $>10^2$ 菌落/ml。

傷口培養：

- 必須要有膿液或紅腫熱痛存在，不可只是單純的根據傷口培養結果用藥。

De-Escalation Therapy (降階治療)

**Initial adequate broad-spectrum therapy
follow by antibiotic de-escalation**

減少不必要的抗生素
以避免抗藥性
發生

給予足夠的抗生素以
改善患者預後

一旦培養出較不抗藥之致病菌則應考慮降階治療



WORLD HEALTH ORGANIZATION

ESSENTIAL DRUGS MONITOR

DOUBLE ISSUE – N° 28 & 29 (2000)

Essential Drugs Monitor

The Essential Drugs Monitor is produced and distributed by the WHO Department of Essential Drugs and Medicines Policy (EDMP). It is published in Chinese, English, French, Spanish and Russian, and has a global readership of some 300,000 to whom it is free of charge. The Monitor carries news of developments in national drug policies, therapeutic guidelines, current pharmaceutical issues, educational strategies and operational research.

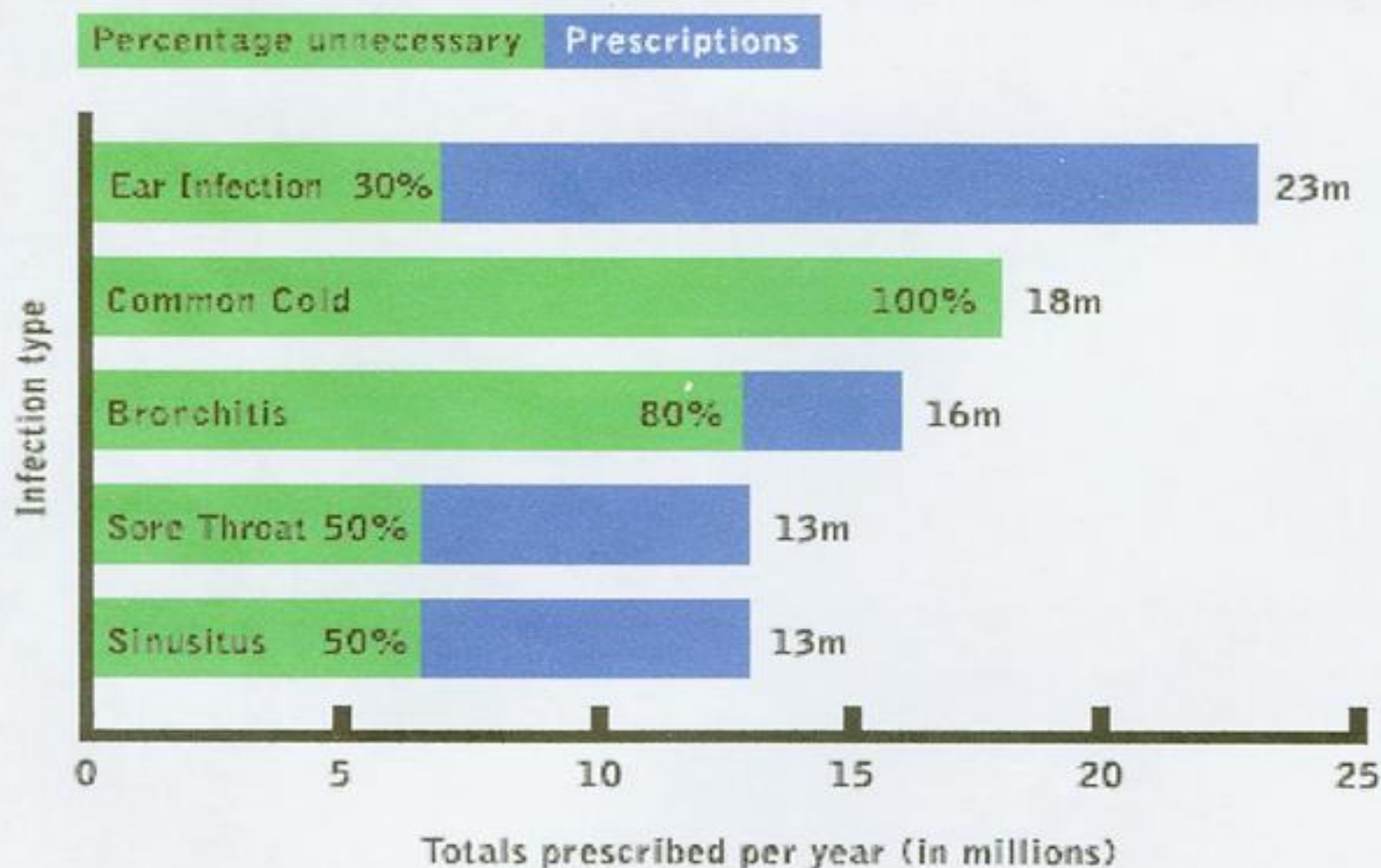
WHO's Department of Essential Drugs and Medicines Policy seeks to ensure that all people – wherever they may be – are able to obtain the drugs they need at a price that they and their country can afford; that these drugs are safe, effective and of good quality; and that they are prescribed and used rationally.

*All correspondence
should be addressed to:*

EDITORIAL

Antimicrobial resistance: a global threat

Unnecessary Antibiotic Prescriptions



NEJM (8/14/97): “In Finland, after nationwide reductions in the use of macrolide antibiotics for outpatient therapy, there was a significant decline in the frequency of erythromycin resistance among group A streptococci isolated from throat swabs and pus samples.”

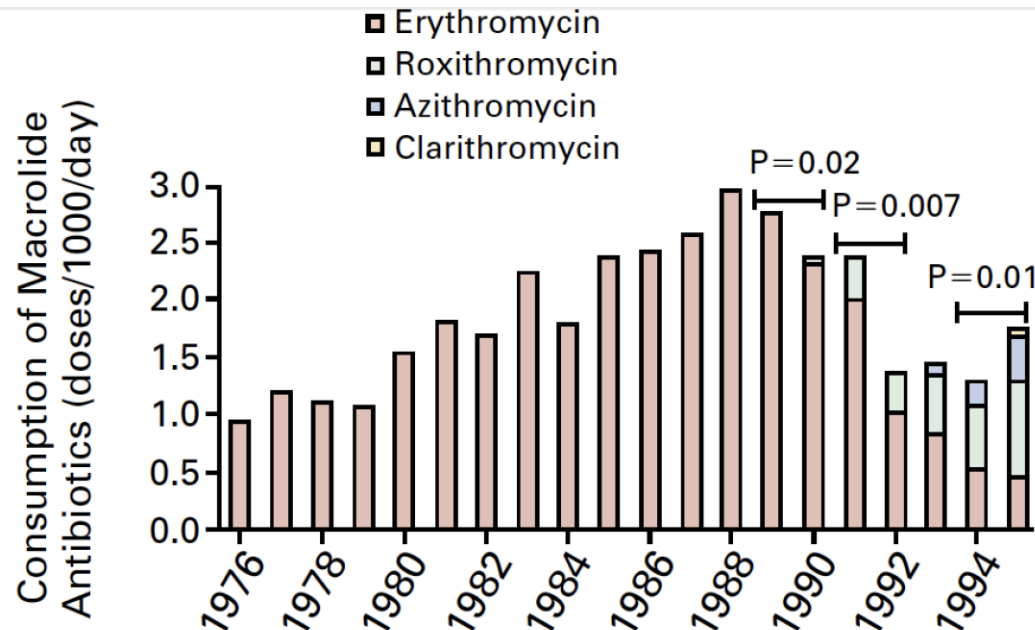


Figure 1. Total Consumption of Macrolide Antibiotics by Outpatients in Finland from 1976 through 1995.

Consumption is expressed in terms of defined daily doses per 1000 inhabitants per day.

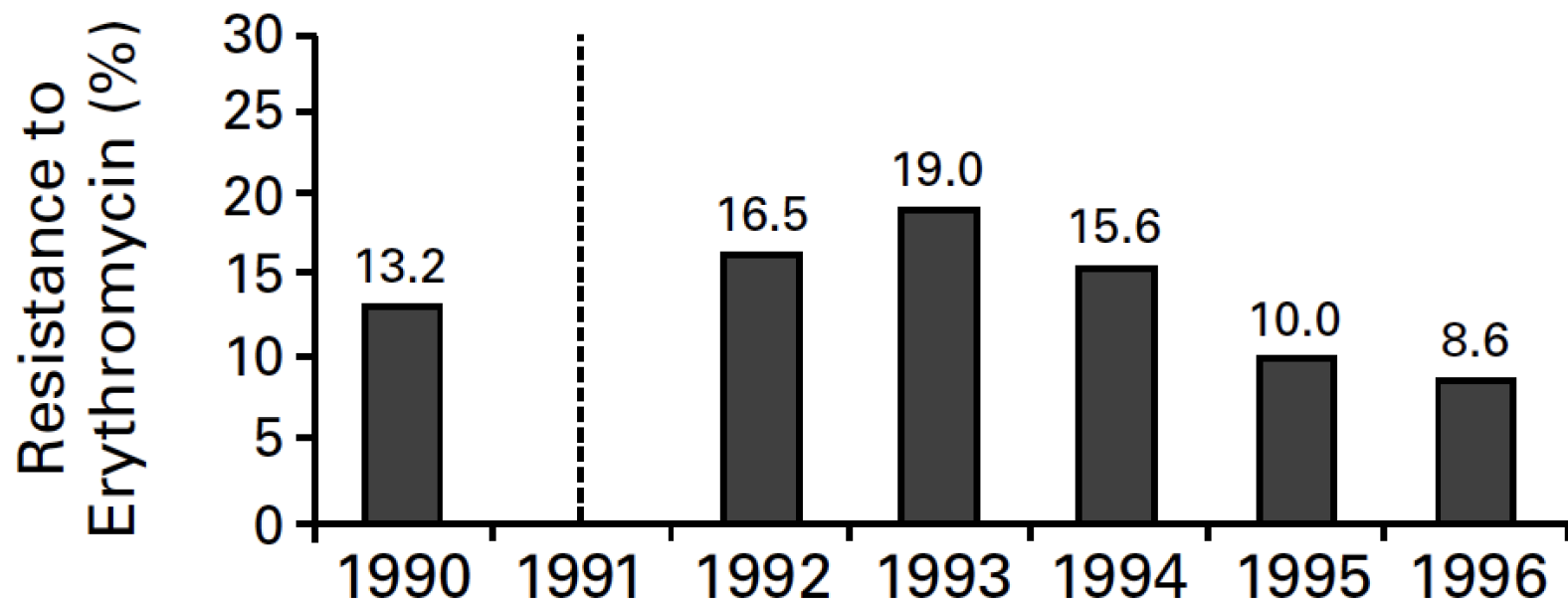
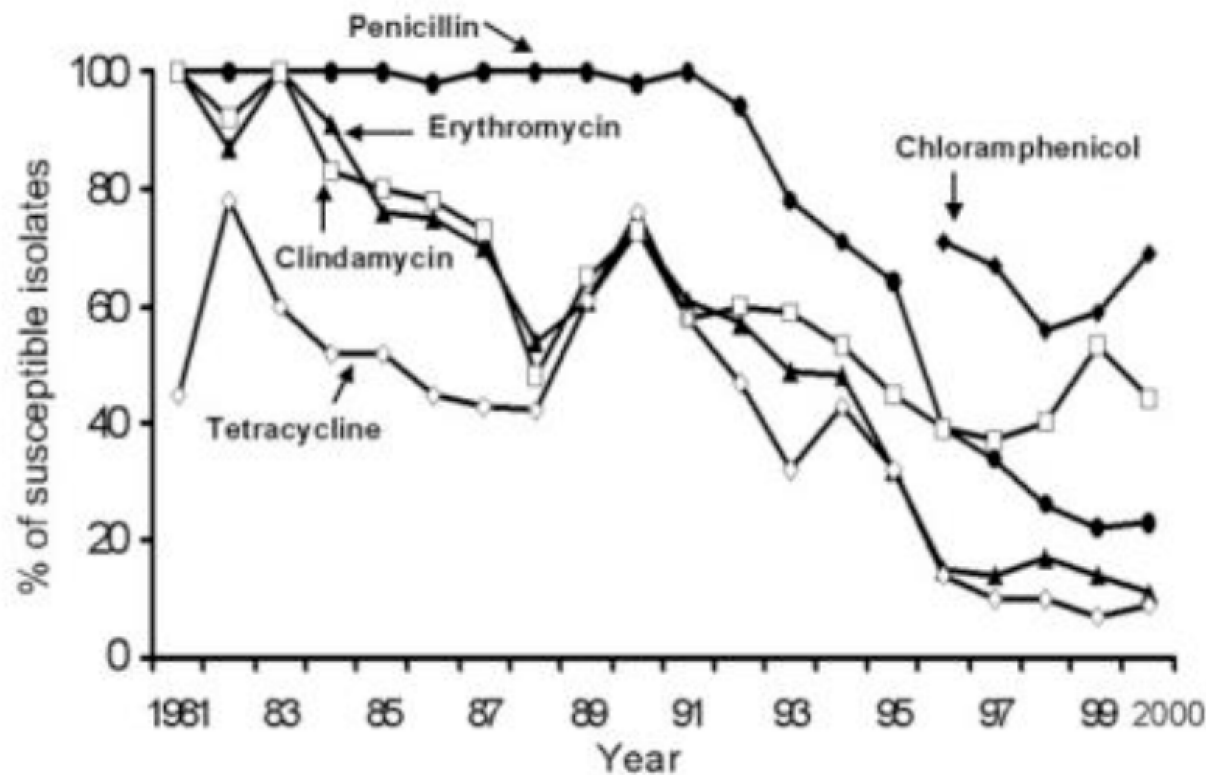


Figure 2. Frequency of Resistance to Erythromycin among Group A Streptococcal Isolates from Throat-Swab and Pus Samples in Finland in 1990 and in 1992 through 1996.

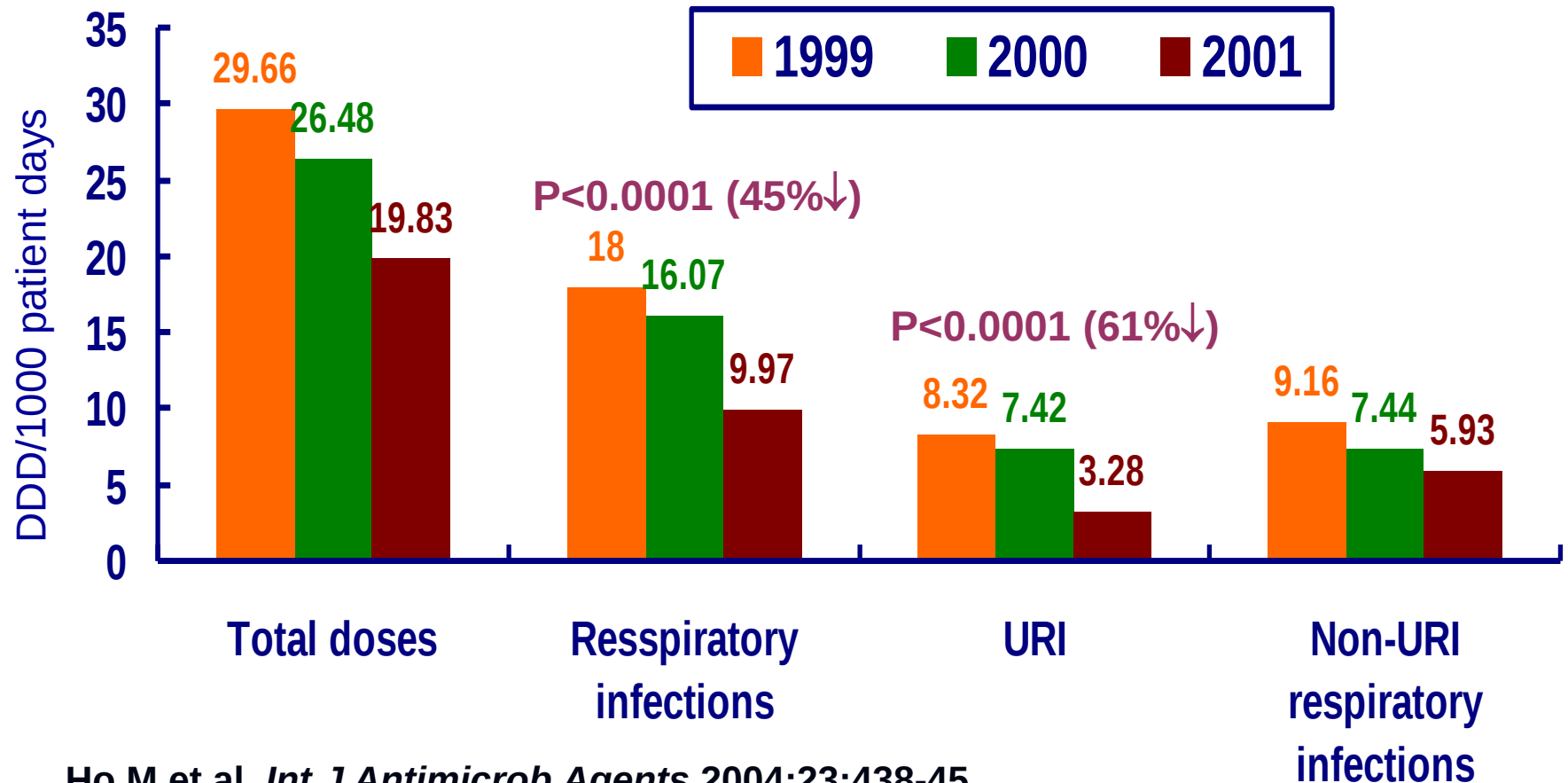


Erythromycin (ERY) resistance among group A *Streptococcus* (GAS) isolates in Taiwan declined from 53.1% in 1998 and 2000 to 14.6% in 2002 and 2004 and 10.7% in 2006 to 2010 ($P < 0.01$) --Taiwan Surveillance of Antimicrobial Resistance (TSAR)

Prevalence of susceptibility to five antimicrobial agents for *Streptococcus pneumoniae* isolates at the National Taiwan University Hospital, 1981–2001.

Changes before and after A Policy to Restrict Antimicrobial Usage in URI

Start 1 February 2001

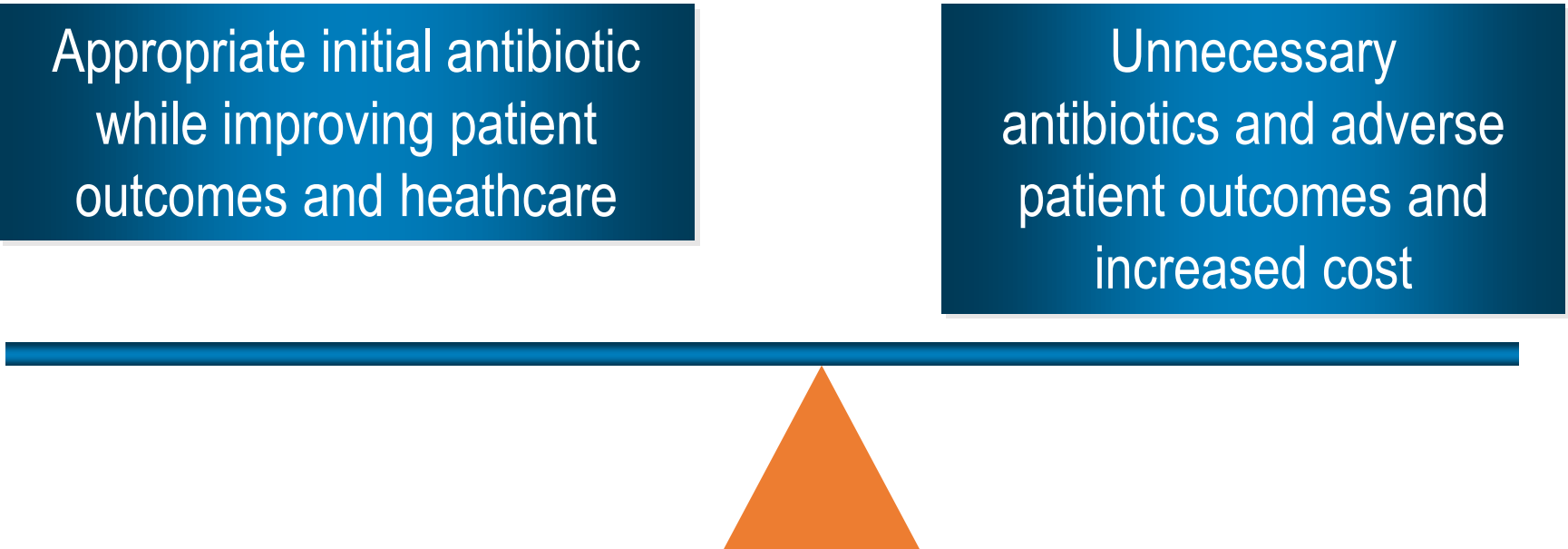


Ho M et al. *Int J Antimicrob Agents* 2004;23:438-45.

Antimicrobial Therapy

Appropriate initial antibiotic
while improving patient
outcomes and healthcare

Unnecessary
antibiotics and adverse
patient outcomes and
increased cost



A Balancing Act

臨床醫師對多重抗藥菌種的因應

ORIGINAL INVESTIGATION

Clinicians' Perceptions of the Problem of Antimicrobial Resistance in Health Care Facilities

Tara Bridget Giblin, MPH; Ronda L. Sinkowitz-Cochran, MPH; Patricia L. Harris, RN, BSN; Sharon Jacobs, RN, MS, CIC; Kathy Liberatore, RN, BSN, CIC; Marsha A. Palfreyman, RN, MS, CIC; Edward I. Harrison, MBA; Denise M. Cardo, MD; for the CDC Campaign to Prevent Antimicrobial Resistance Team

Table 1. Campaign Strategies and Steps, Campaign to Prevent Antimicrobial Resistance, 12-Step Program for Hospitalized Adults, 2002²¹

Strategy: Prevent Infection

Step 1: Vaccinate

Step 2: Get the catheters out

Strategy: Diagnose and Treat Infection Effectively

Step 3: Target the pathogen

Step 4: Access the experts

Strategy: Use Antimicrobials Wisely

Step 5: Practice antimicrobial control

Step 6: Use local data

Step 7: Treat infection, not contamination

Step 8: Treat infection, not colonization

Step 9: Know when to say “no” to vanco

Step 10: Stop treatment when infection is cured or unlikely

Strategy: Prevent Transmission

Step 11: Isolate the pathogen

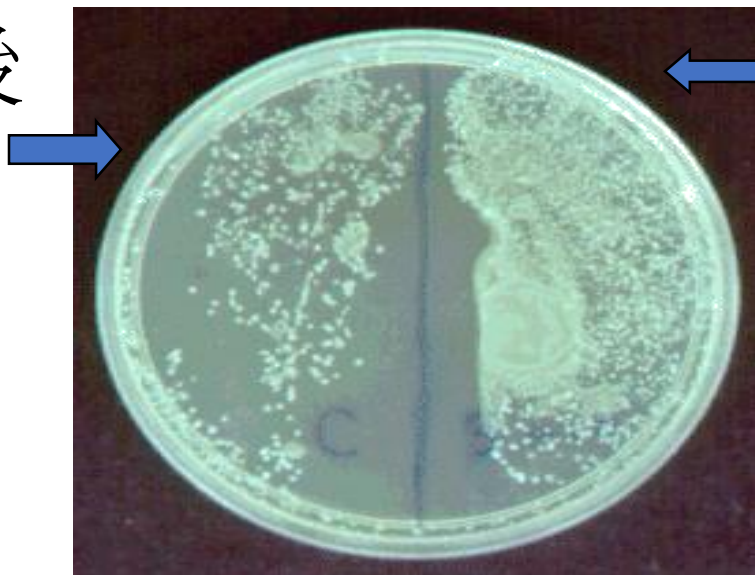
Step 12: Break the chain of contagion

Table 2. Clinicians' Perceptions of the Problem of Antimicrobial Resistance, Campaign to Prevent Antimicrobial Resistance, 12-Step Program for Hospitalized Adults: Questionnaire of 4 Hospitals (Pittsburgh Regional Healthcare Initiative, 2002)*

Response	Antimicrobial Resistance Is a Problem		
	Nationally	In My Institution	In My Practice
Strongly agree	68.1	40.7	40.0
Agree	26.7	36.3	25.3
Neither agree nor disagree	1.7	17.7	22.1
Disagree	0.9	4.4	10.5
Strongly disagree	2.6	0.9	2.1

*Data are given as percentages of perceptions of 117 clinicians.

洗手後



← 洗手前



**Infection Control and Appropriate Use of
Antibiotics are Equal Important!**

謝謝聆聽