ANTIBIOTIC STEWARDSHIP. THE NEED FOR ANTIBIOTIC WISDOM

PRESENTED BY:
Dr: MOSTAQRET ALI
INFECTIUOS DISEASE RESEDENT AT HADASSAH HOSPITAL

Menu for this afternoon:

- MDR among patients who get therapy at Hadassah medical center (2009-2011) , Study
- Resistance issue
- Antibiotic stewardship, importance and challenges
- Summary and home messages

MEDICAL TOURISM AS A SOURCE FOR MULTIDRUG RESISTANT PATHOGENS – A COHORT ANALYSIS

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OBJECTIVES

Aims were:

- 1.To estimate the prevalence of MDR-CP among this population in comparison to Israeli patients.(**Eastern Europe medical tourists and patients from the Palestinian authority**).

- 2.To assess the need for screening upon admission and/or preemptive isolation pending results.

METHODS

- All patients admitted to Hadassah Medical Center Jerusalem between 2009 and 2011, from whom any cultures were obtained, were included.

four groups:

1. Israeli residents,
2. East Jerusalem residents (Palestinians, who are served mainly by Israeli health services),
3. Palestinian patients
4. Foreign patients.

- Only specimens collected within 96 hours of hospital admission were included in the analysis.

- **MDR-CP**:

a) carbapenem-resistant *A. baumannii and Enterobacteriaceae,*
b) *vancomycin-resistant Enterococci,(VRE)*
c) *methicillin-resistant Staphylococcus aureus (MRSA)*
a) *C. difficile.*

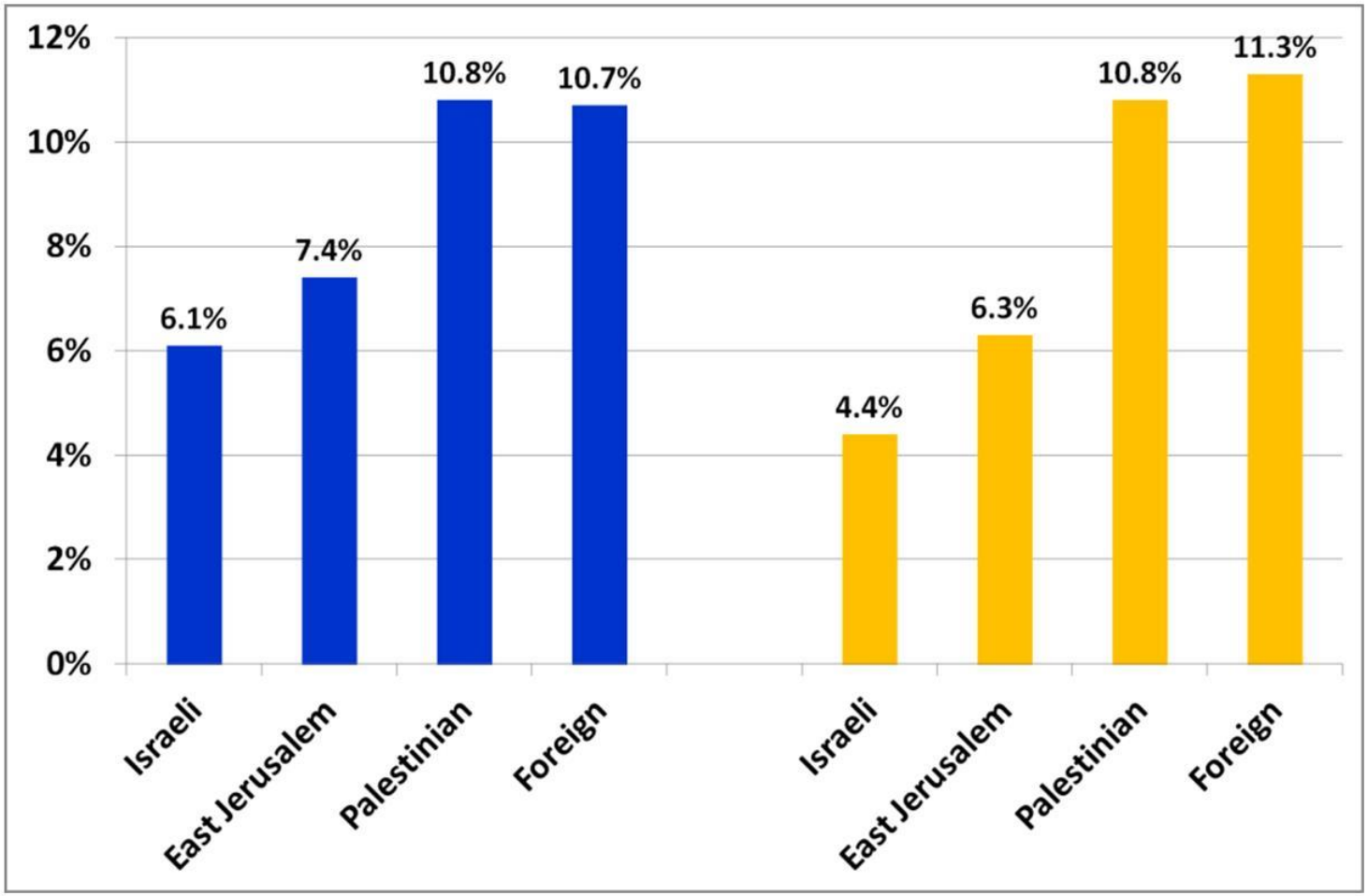
RESULTS :

- 906/14,122 (6.4%) positive cultures obtained within 96 hours from admission met the criteria of MDR-CP

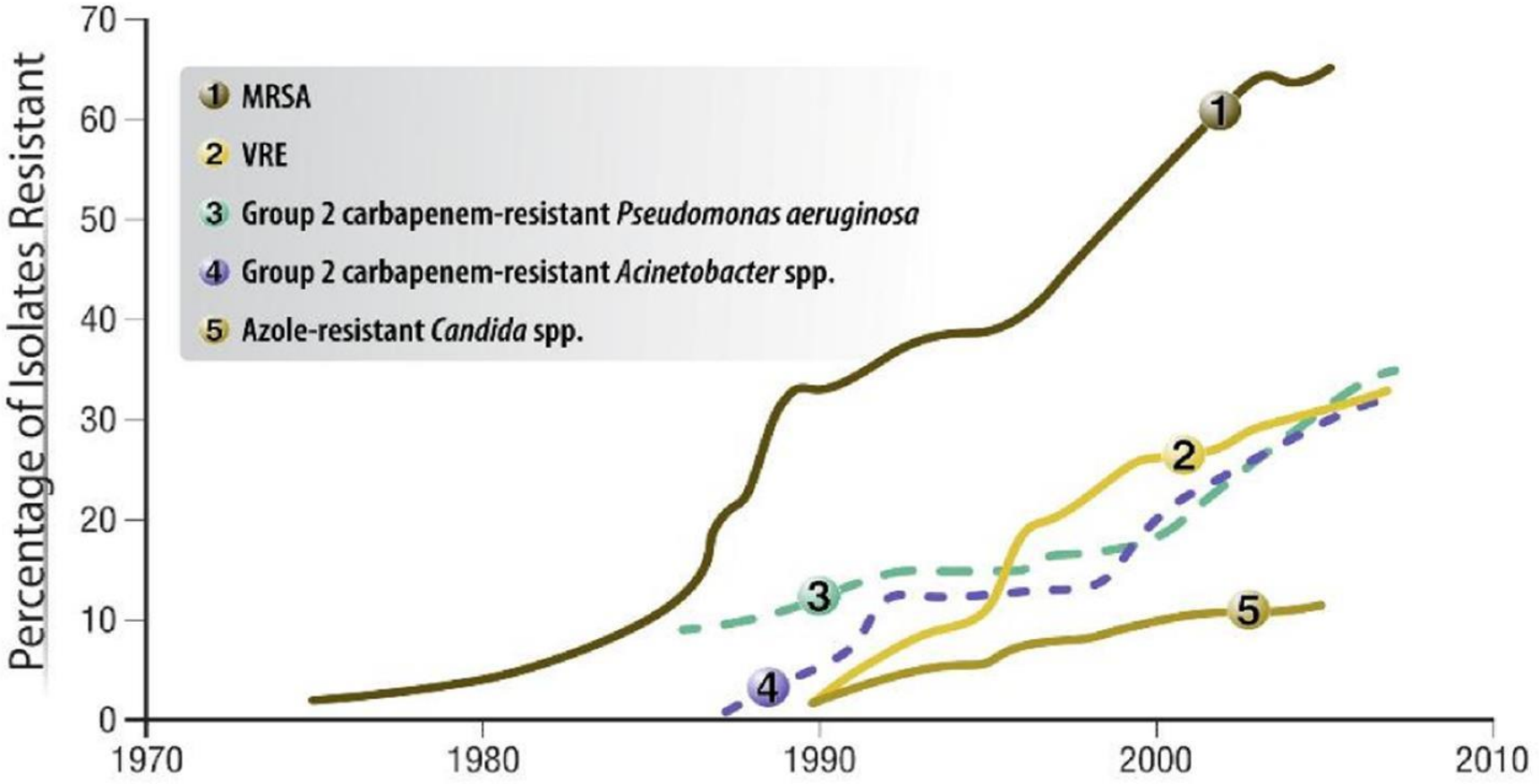
- Rates of MDR CP according to the different population groups were as follows: **Israeli residents (6.1%), East Jerusalem (7.4%), Palestinian patients (10.8%) and foreign patients (10.7%) (p<0.001).**

ALL AGE GROUPS (P<0.001)

<75 YEARS (P<0.001)



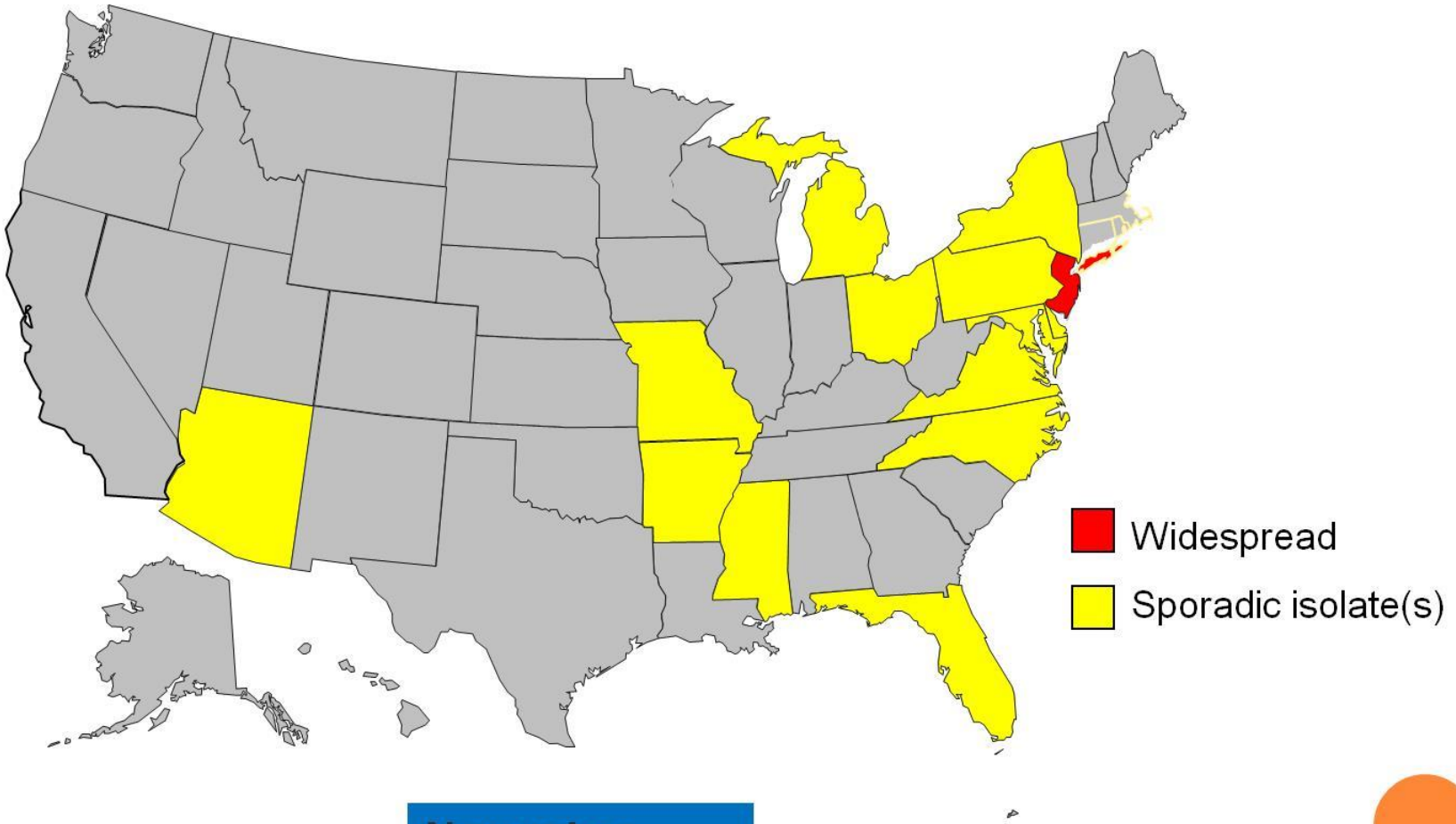
Trends in Antimicrobial Resistance



Adapted from Wenzel RP, et al. *Infect Control Hosp Epidemiol.* 2008;29:1012-1018.

Geographical Distribution of KPC(CRE)-Producers

IMET2000-Pal
www.imet2000-pal.org

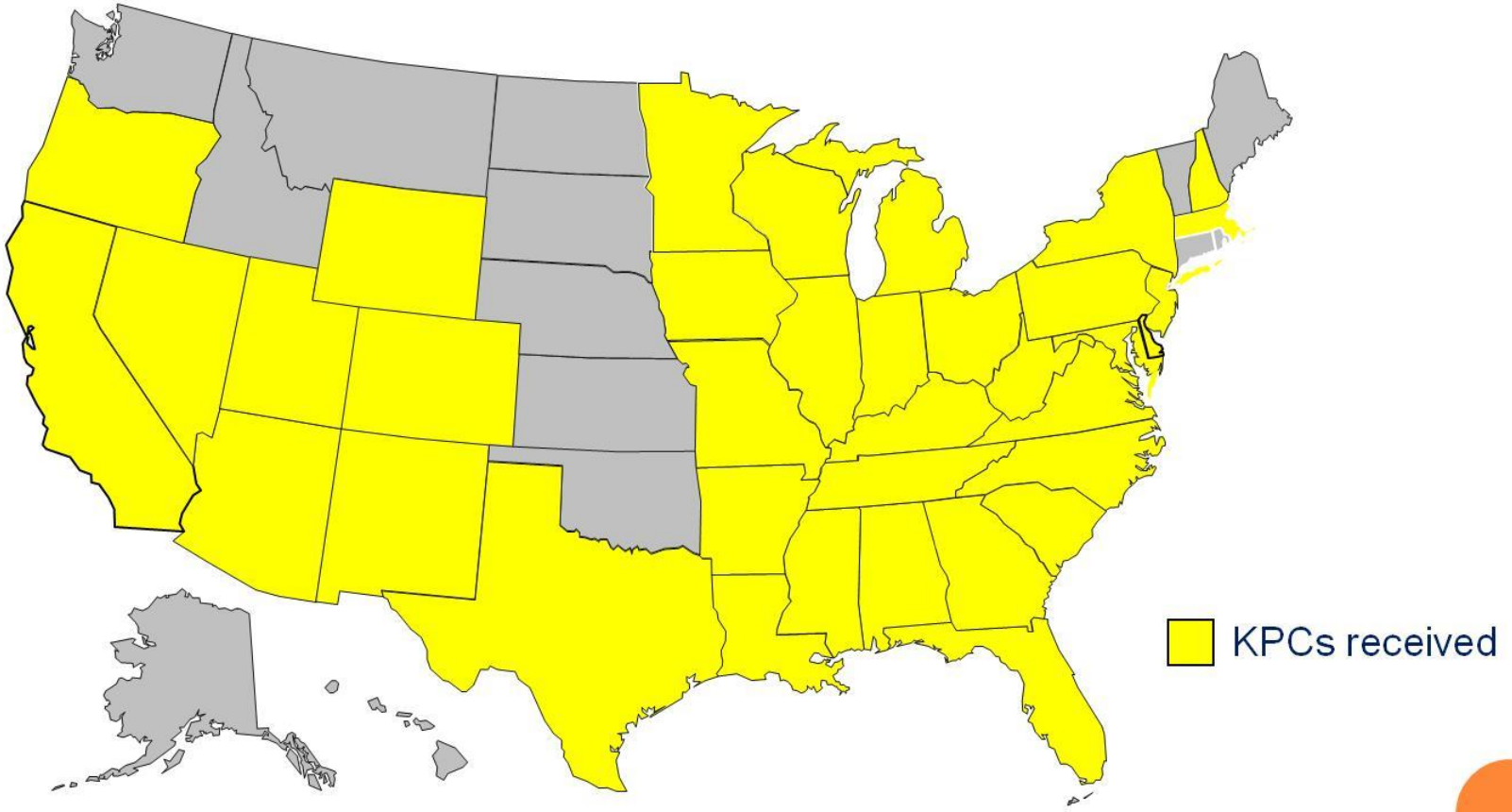


November 2006

Centers for Disease Control and Prevention.

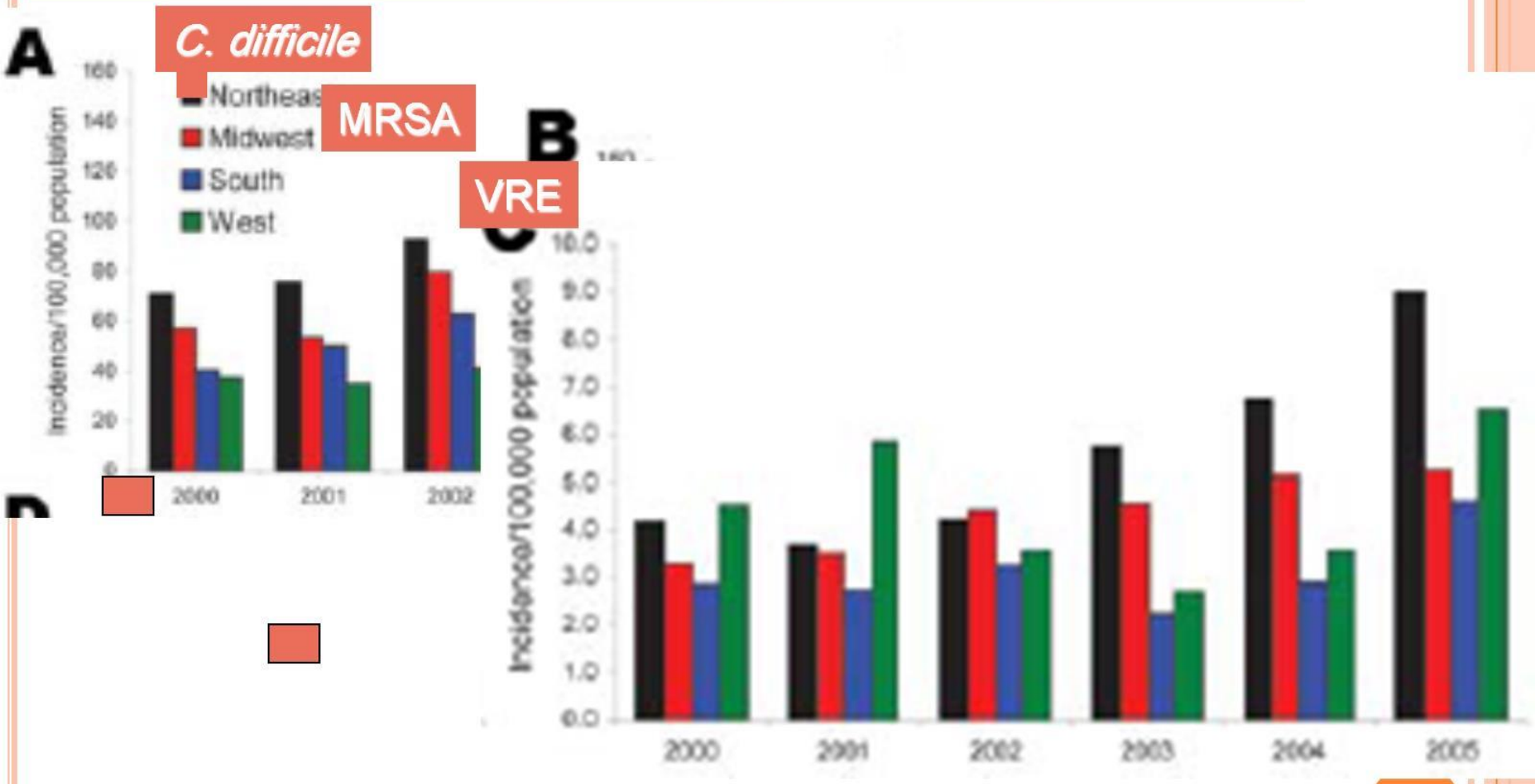
GEOGRAPHICAL DISTRIBUTION OF EXTREME-DRUG RESISTANT *KLEBSIELLA* BACTERIA

IMET2000-Pal
www.imet2000-pal.org



August 2010

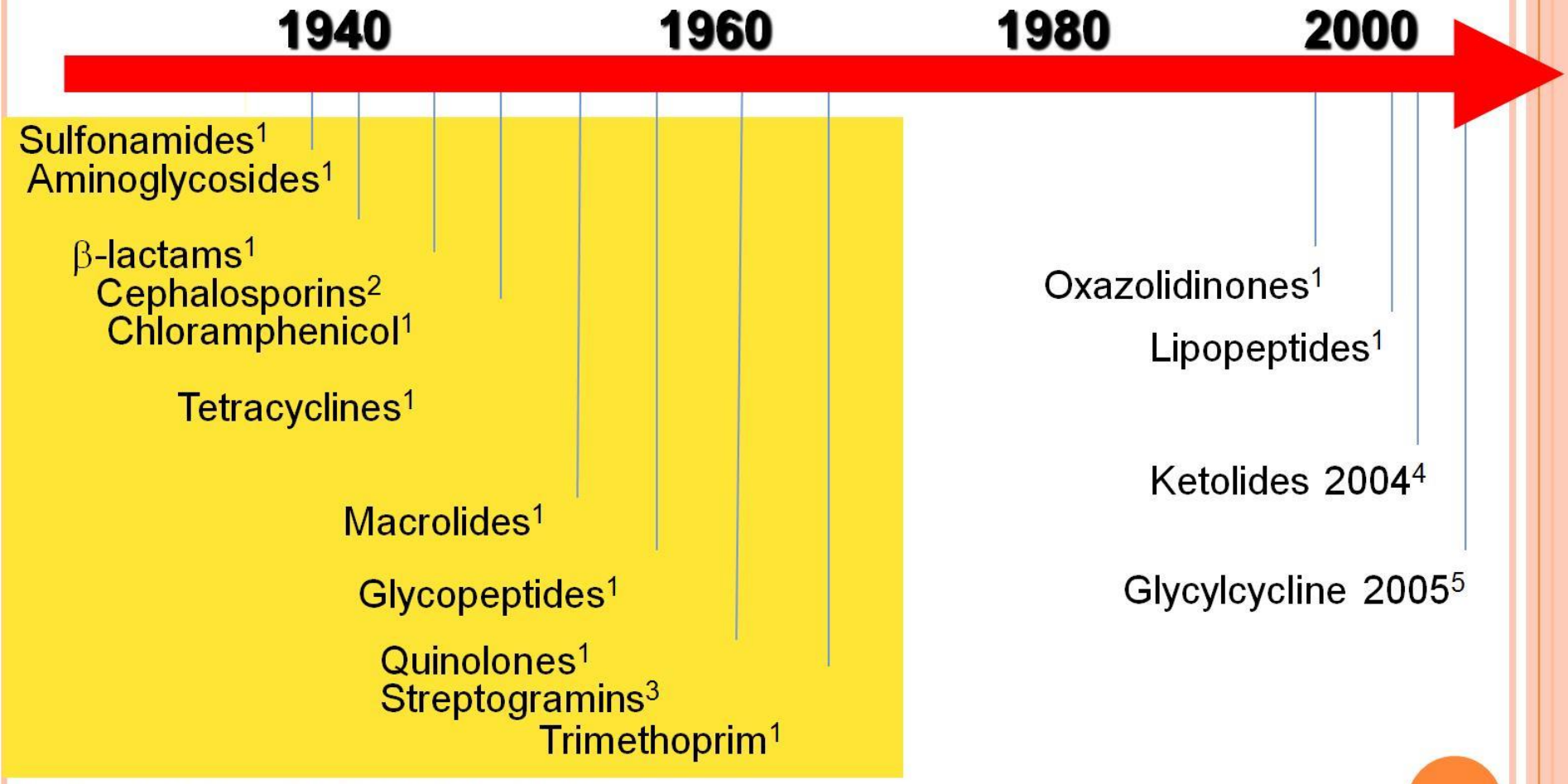
Progression of Resistance – U.S.



Data taken from the National Inpatient Sample data available on the Healthcare Costs and Utilization Project net [HCUPnet] website, administered by the Agency for Healthcare Research and Quality.
Zilberberg MD, et al. *Emerg Infect Dis.* 2008;14:1756-1758.

- So, we have an increase trend of microorganisms resistance.
- **Is it that the whole issue??**
- What about our Weapon???

Introduction of New Antibiotic Classes

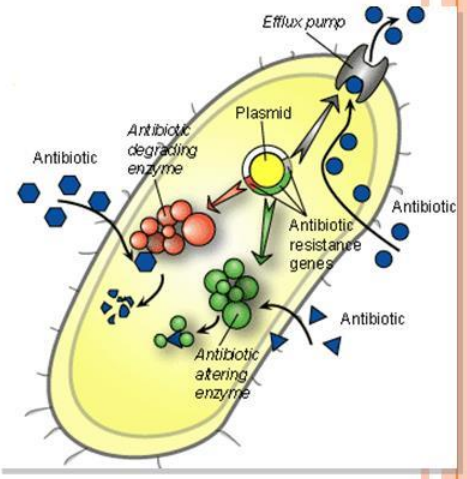


1. Wenzel RP. *N Engl J Med.* 2004;351:523-526.
2. Jantausch BA. *Pediatr Rev.* 2003;24:128-136.
3. Khardori N. *Med Clin North Am.* 2006;90:1049-1076.
4. FDA. *Antimicrob Agents Chemother.* 2005;49:2151.
5. Peterson LR. *Clin Infect Dis.* 2006;42:224-33.

We Have a Basic Problem

New Drug Discovery

Rates of Resistance



The Octopus of Multi-Drug Resistance (MDR)

In short…we have a problem !

- Growing rates of resistance
- Inappropriate use
- Decreasing pipeline of new antibiotic

RESEARCH

Staphylococcus aureus bacteraemia: a major cause of mortality in Australia and New Zealand

John D Turnidge, Despina Kotsanas, Wendy Munckhof, Sally Roberts, Catherine M Bennett, Graeme R Nimmo, Geoffrey W Coombs, Ronan J Murray, Benjamin Howden, Paul D R Johnson and Kate Dowling
on behalf of the Australia New Zealand Cooperative on Outcomes in Staphylococcal Sepsis

ABSTRACT

Objective: To document the types of, and mortality from, *Staphylococcus aureus* bacteraemia in Australia and New Zealand, and determine factors associated with mortality.

Design and setting: Prospective observational study in 27 independent or hospital pathology laboratories in Australia (24) and New Zealand (3), employing a web-based database to prospectively record demographic features, selected risk factors, principal antibiotic treatment and mortality data on all patients with positive blood cultures for *S. aureus* from June 2007 to May 2008.

Main outcome measure: 30-day all-cause mortality.

Results: 1994 episodes of *S. aureus* bacteraemia were identified, and complete 30-day follow-up data were available for 1865. Most episodes had their onset in the community (60.8%; 95% CI, 58.7%–63.0%). Methicillin-resistant *S. aureus* (MRSA) caused 450 episodes (24.1%; 95% CI, 22.2%–25.9%), and 123 of these (27.3%) had a susceptibility profile consistent with community-associated MRSA. All-cause mortality at 30 days was 20.6% (95% CI, 18.8%–22.5%). On univariate analysis, increased mortality was significantly associated with older age, European ethnicity, MRSA infection, infections not originating from a medical device, sepsis syndrome, pneumonia/empyema, and treatment with a glycopeptide or other non-β-lactam antibiotic. On multivariable analysis, independent predictors of mortality were age, sepsis syndrome, pneumonia/empyema, device-associated infection with a secondary focus, left-sided endocarditis, and treatment with a glycopeptide such as vancomycin, but not MRSA infection.

Conclusions: *S. aureus* bacteraemia is a common infection in both the community and hospitals in Australia and New Zealand, and is associated with appreciable mortality. Invasive MRSA infection may be more life-threatening, partly because of the inferior efficacy of the standard treatment, vancomycin. National web-based surveillance of *S. aureus* bacteraemia and its outcomes is not only important but also easily achievable.

MJA 2009; 191: 368–373

For editorial comment, see page 363. See also page 389.

Staphylococcus aureus sepsis, especially that caused by methicillin-resistant *S. aureus* (MRSA), is widely recognised by the public and the general medical community as a problem associated with health care. Less well recognised, but equally important, is invasive *S. aureus* infection arising in the community. The emergence of community strains of MRSA has added significant concern about community-onset infections.[1] Although there is a wide variety of manifestations of serious invasive infections caused by *S. aureus*, in the great majority of these cases, the organism can be detected in blood cultures. Therefore, *S. aureus* bacteraemia is considered a very useful marker for these serious invasive infections,[2] and in some cases, is the only initial manifestation of the infection.

Published reports of experience around the world show that mortality from infections associated with *S. aureus* bacteraemia can range from as low as 2.5% to as high as 40%.[3-5] Mortality rates are known to vary significantly with patient age, clinical manifestation and comorbidities. Until recently, there have been no national data on the incidence and outcomes of *S. aureus* bacteraemia in either Australia or New Zealand. Small, largely retrospective, studies have been conducted, usually in single institutions. A recent prospective study of *S. aureus* bacteraemia conducted in 17 sites across Australia found a crude mortality rate of 11.2% when measured at discharge or 7 days, whichever came sooner.[6] An earlier study that documented outcomes in six major centres in New Zealand found an all-cause mortality of 22.4% and an attributable mortality of 18.9%.[7]

The Australia New Zealand Cooperative on Outcomes in Staphylococcal Sepsis (ANZCOSS) was established in 2007 to prospectively examine mortality from infections associated with *S. aureus* bacteraemia in a more structured way and to determine some of the risk factors for poor outcomes.[8]

METHODS

Independent or hospital pathology laboratories in Australia and New Zealand were asked to join the cooperative on a voluntary basis. Invitations were extended to all members of the Australian Group on Antimicrobial Resistance,[9] and by open invitation to selected hospital laboratories in New Zealand. The entry criterion for participating sites was a single blood culture that tested positive for *S. aureus*, associated with clinical manifestations in the patient consistent with staphylococcal infection. The date of study entry was the date of collection of the first positive culture in an episode of infection. A new episode in the same patient was recorded if the bacteraemia had cleared, but a further culture of blood taken more than 14 days after the initial positive culture was again positive.

Approval to conduct the prospective data collection was given by the research ethics committee associated with each participating laboratory. A web-based data entry system was constructed to enable real-time data collection into a common database. To ensure patient anonymity, but to allow follow-up of discrepant results with each participating site, a record identifier unique to the participating site was used. Data were collected on age, sex, ethnicity, date of admission (if admitted), date of discharge, relationship of the infection to a medical device and its type, the principal clinical manifestation of the infection, the principal agent used for definitive initial treatment (usually intravenous), and mortality at 7 and 30 days from date of entry. To avoid interpretive bias, no attempt was made to assign attributable mortality. Participating sites

???....

Facility-Level Prevention Strategies Acute and Long-Term Care

- Core Measures
  - Hand Hygiene
  - Contact Precautions
  - Healthcare Provider (HCP) Education
  - Minimize Device Use
  - Patient and Staff Cohorting
  - Laboratory Notification
  - Antimicrobial Stewardship
  - CRE Screening

THE JOURNAL OF INFECTIOUS DISEASES • VOL. 157, NO. 5 • MAY 1988
 0022-1899/88/5705-0002$01.00

From the Infectious Diseases Society of America

Society for Healthcare Epidemiology of America and Infectious Diseases Society of America Joint Committee on the Prevention of Antimicrobial Resistance: Guidelines for the Prevention of Antimicrobial Resistance in Hospitals

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Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship

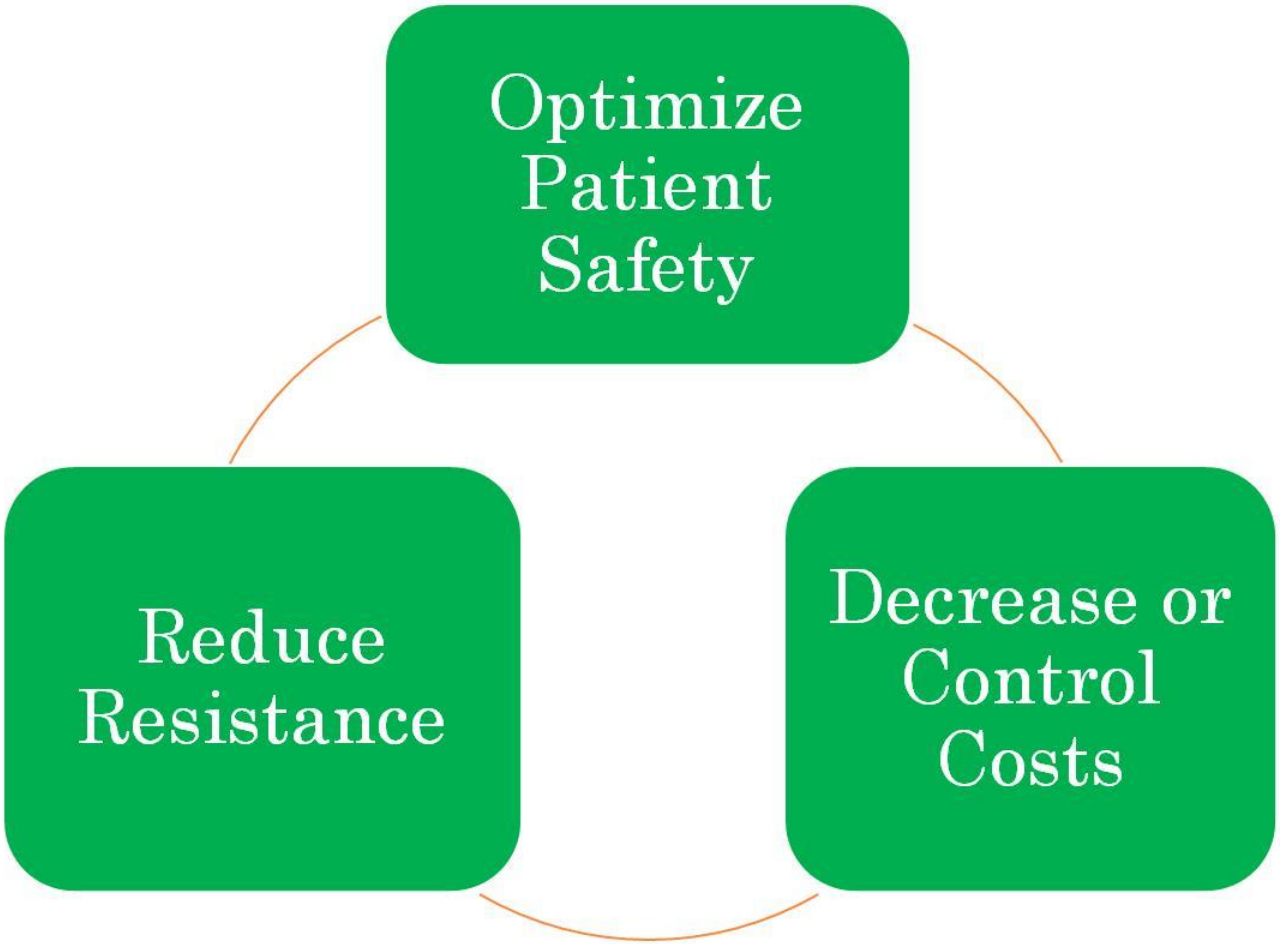
Timothy H. Dellit,[1] Robert C. Owens,[2] John E. McGowan, Jr.,[3] Dale N. Gerding,[4] Robert A. Weinstein,[5] John P. Burke,[6] W. Charles Huskins,[7] David L. Paterson,[8] Neil O. Fishman,[9] Christopher F. Carpenter,[10] P. J. Brennan,[9] Marianne Billeter,[11] and Thomas M. Hooton[12]

Antibiotic Stewardship

- Optimize clinical outcomes while minimizing unintended consequences of antibiotic use
  - Toxicity
  - Selection of pathogenic organisms
  - Emergence of resistance
- Combine with comprehensive infection control to limit emergence and transmission of resistance
  - Reduce health care costs without adversely impacting quality of care

Dellit TH, et al. *Clin Infect Dis*. 2007;44(2):159-177.

Goals of Antimicrobial Stewardship Programs



Empiric Antimicrobial Therapy : A Balancing Act

Rapid, effective therapy

Unnecessary therapy,
Collateral damage

Defining Appropriate Therapy

Considerations in determining appropriate therapy:

- **Spectrum of activity**
- **Timing of therapy**
- **Dose and dosing frequency.**
- **Drug interactions and tolerability**
- **Adequate drug levels**
- **Prior antibiotic treatment**
- **Potential for engendering antibiotic resistance**

Raymond DP et al. *Surg Infect* 2002;3:375-385.

Moellering RM. In: GL Mandell, JE Bennett, R Dolin, eds. *Principles and Practice of Infectious Diseases*, 5th ed, 2000.

Fry DE. *Surg Infect* 2001;2:S3-S11.

MDR Risk Factors

- Hospital LOS*
- ICU LOS*
- Central venous catheters
- Arterial catheters
- Emergent abdominal surgery
- Gut colonization
- Presence jejunostomy or gastrostomy tube
- Prior antibiotics
- Residence in long-term care facility*
- Severity of illness
- Presence of urinary catheter
- Hemodialysis*
- Ventilatory assistance

At the A. Fleming School for Budding Bacteria, "Germ Culture" is taken very seriously.

Data Support Antimicrobial Stewardship

- 36 published studies on effect of antimicrobial stewardship

- Cost: 27 of 29 demonstrated a reduction
- Resistance: 22 studies with positive effects on multiple organisms/drugs including C. diff
- Adverse Effects: 1 of 2 demonstrated improvement

Patel D et al. *Expert Review of Anti-Infective Therapy* 2008

Key Members of the Team

Multidisciplinary team

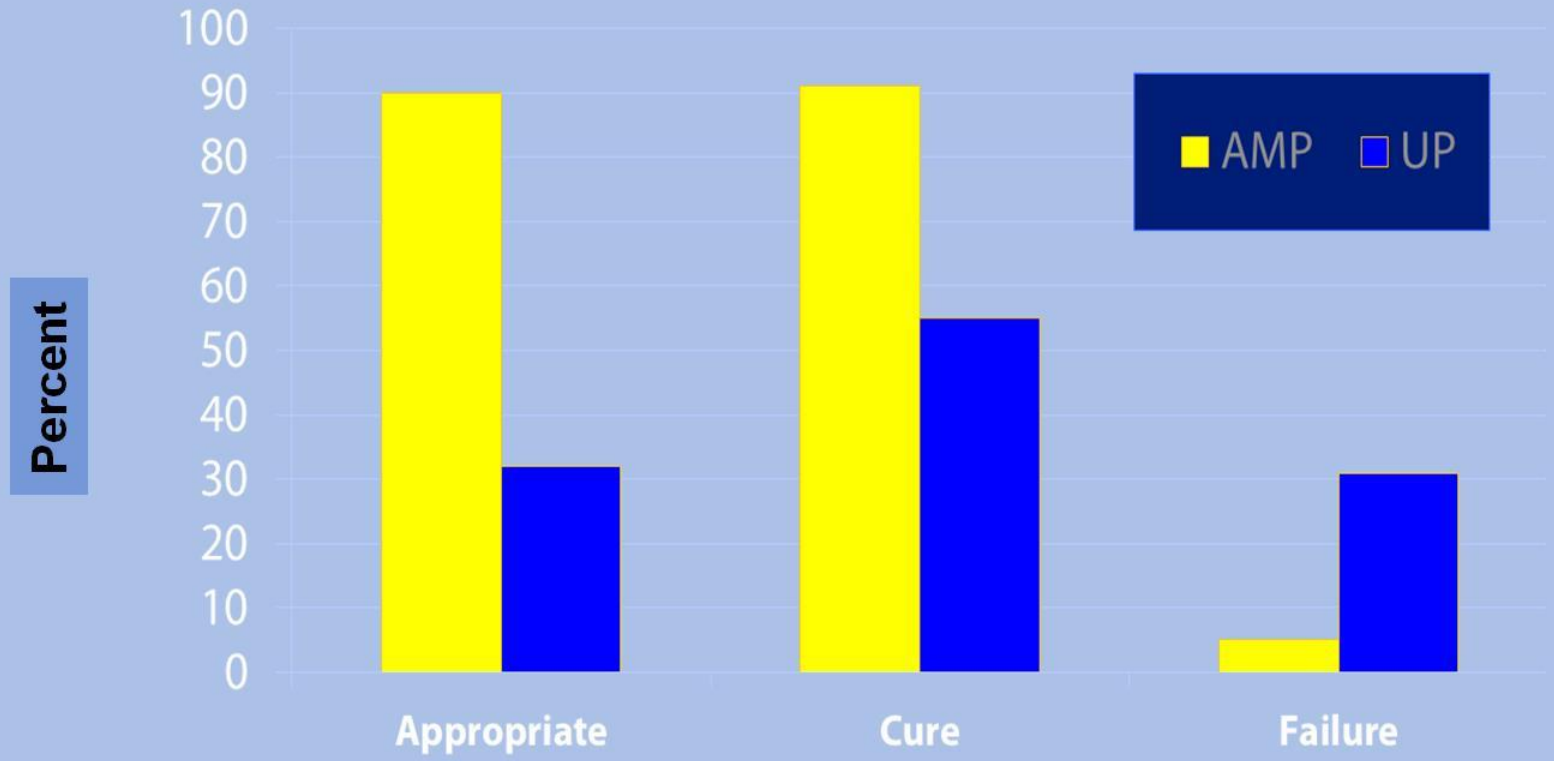
- Infectious Diseases physician(s)
- ID Pharmacist
- Microbiology
- Administration (support, agree with metrics and goals)
- Informatics support

A "Rational" Stewardship Strategy

- Broad spectrum therapy for empiric treatment of suspected invasive nosocomial infection
- Rapid de-escalation by day 3-4
- When possible, short durations of in-hospital antibiotics for selected populations
- Avoid anti-pseudomonal agents when possible

"Hit hard, de-escalate, get out"

Antibiotic Stewardship Improves Clinical Outcomes



RR 2.8 (2.1-3.8)

RR 1.7 (1.3-2.1)

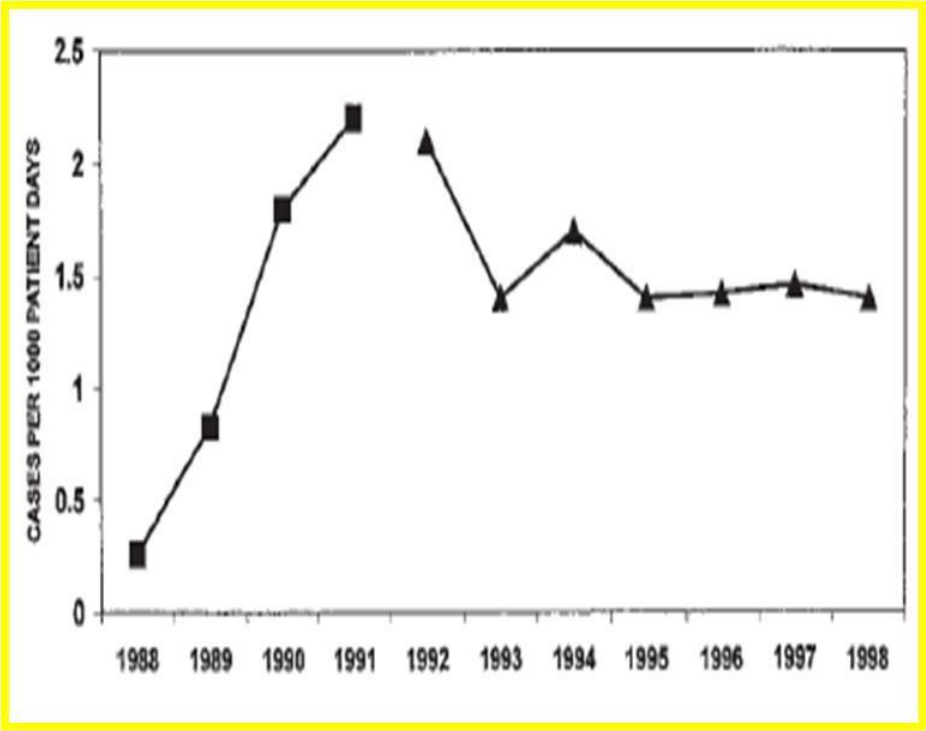
RR 0.2 (0.1-0.4)

AMP = Antibiotic Management Program
UP = Usual Practice

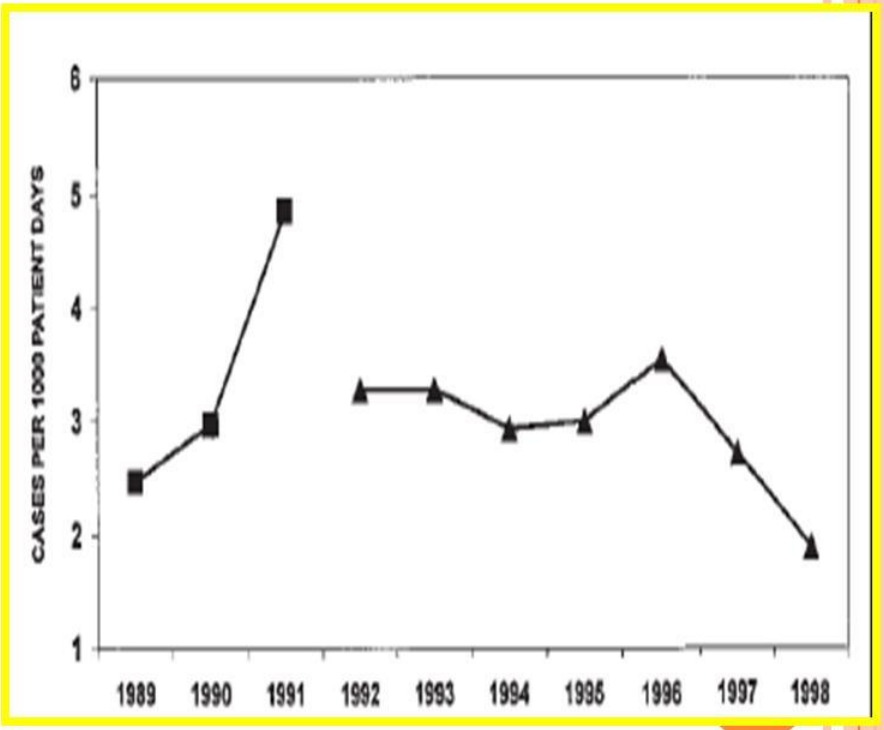
Fishman N. *Am J Med* 2006;119:S53.

Antibiotic Stewardship Reduces *C. difficile* Infection and Gram Negative Resistance

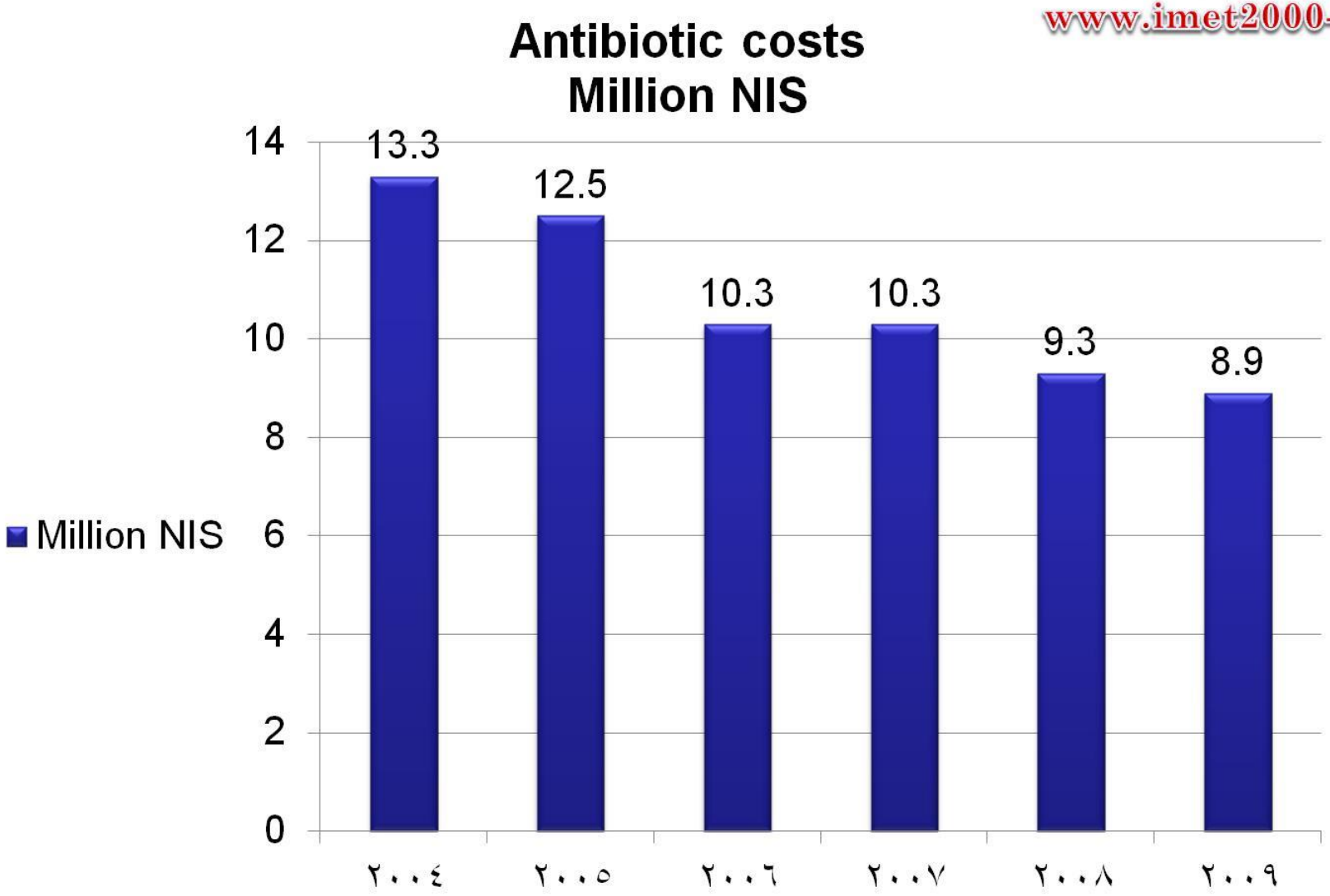
Rates of *C. difficile* AAD



Rates of Resistant Enterobacteriaceae



Carling P et al. Infect Control Hosp Epidemiol. 2003;24(9):699-706.



Conclusion

- The therapeutic benefit of antibiotics should be balanced with their unintended adverse consequences
- Inappropriate antibiotic use is associated with increased antibiotic resistance, adverse drug effects and *Clostridium difficile* infection
- Antibiotic stewardship is important for preserving existing antibiotics and improving patient outcomes

Remember….

- **Antibiotic resistance is a global problem**
- **Resistant infections are harder to treat and are associated with higher rates of mortality and morbidity**
- **Inappropriate use of antibiotics drives resistance**
- **If we don't all take action today, there may be *no cure tomorrow*…**

Take home messages

1. Obtain cultures before starting therapy
2. Use *Therapeutic Guidelines: Antibiotic*[17]
3. Document indication and review date
4. Review and reassess antibiotics at 48 hours
5. Consider IV to oral switch
6. Seek advice for complex cases

Bad Bugs, No Drugs

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

"Bad Bugs, No Drugs." IDSA. July 2013

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