

# Infections due to Multi-Drug Resistant (MDR) Gram-Negative Pathogens

## Prof. Keith Kaye, Wayne State University

### Broadcast live from the 2012 APIC conference (www.apic.org)

**Infections due to Multi-Drug Resistant (MDR) Gram-Negative Pathogens Across the Continuum of Care**

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BROADCAST LIVE FROM




www.webbertraining.com June 5, 2012

**Overview**

- MDR Gram-negative bacilli (GNB) of interest
- Role of long-term care and the community in the spread of MDR GNB
- Methods to control the spread of MDR GNBs
- Challenges and opportunities for future management and control

**Bad Bugs, No Drugs: No ESKAPE! An Update from the Infectious Diseases Society of America**

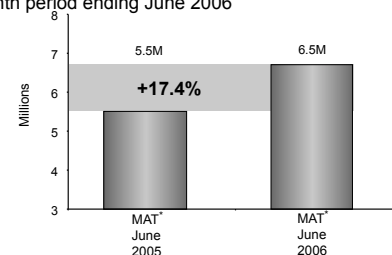
Helen W. Boucher,<sup>1</sup> George H. Talbot,<sup>2</sup> John S. Bradley,<sup>3\*</sup> John E. Edwards, Jr.,<sup>4,5\*</sup> David Gilbert,<sup>6</sup> Louis B. Rice,<sup>7\*</sup> Michael Scheil,<sup>8</sup> Brad Spellberg,<sup>9,10</sup> and John Bartlett<sup>11</sup>

- **Bad Bugs, No Drugs: No ESKAPE**
  - *Enterococcus faecium* (E), *Staphylococcus aureus* (S), *Klebsiella pneumoniae* (K), *Acinetobacter baumannii* (A), *Pseudomonas aeruginosa* (P), and *Enterobacter* spp. (E)
- The late-stage clinical development pipeline remains unacceptably lean
  - Some important molecules for problematic pathogens such as MRSA
  - Few novel molecules for other ESKAPE pathogens
  - No new drugs for infection due to multidrug-resistant Gram-negative bacilli (eg, *A. baumannii* and *P. aeruginosa*)
  - None represent more than an incremental advance over currently available therapies

Clinical Infectious Diseases 2009;48:1-12

**Commonly Used Antibacterials for Serious Infections Are Being Challenged**

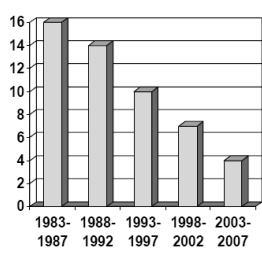
- Days of carbapenem therapy increased 17.4% in a 12-month period ending June 2006



Period	Millions
MAT June 2005	5.5M
MAT June 2006	6.5M

\*MAT = moving annual total.  
 1. Arlington Medical Resources Inc. (AMR) 2006. Total carbapenem days of therapy growth.

**Total Approved Antibacterials: US**



Year Range	Total # New Antibacterial Agents
1983-1987	~15
1988-1992	~14
1993-1997	~10
1998-2002	~7
2003-2007	~4

Spellberg, et. al., CID May 1 2004, Modified

**MDR GNB Pathogens of Interest**

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Extended-spectrum  $\beta$ -lactamases (ESBLs):  
The Forgotten (and Underrated) MDR GNB

- Most commonly identified in enterobacteriaceae
- Plasmid-mediated
- Impart decreased susceptibility to  $\beta$ -lactam antimicrobials
  - Often co-resistance to aminoglycosides, fluoroquinolones
- Carbapenems are drugs of choice for invasive infections due to ESBL-producers

### CTX-M: ESBL Epidemic

- Common ESBL worldwide, often produced by *Escherichia coli*
- Often causes UTI
- Now reported in US
  - Healthcare associated
  - Some community
- Community-based ESBL infection raise concern for continued increases in carbapenem use

Urban, *Diag Micro Infect Dis*, 2010; Sjölund-Karlsson, *EID*, 2011

### The CTX-M Detroit Experience

- From 2006-2011, total number of ESBL-producing *E. coli* increased from
  - 1.9% of all *E. coli* tested to 13.8% of all *E. coli* tested
- From 2/11-7/11 at Detroit Medical Center, 575 cases of ESBL-producing *E. coli* were identified
  - 82% urine
  - 8% wound
  - 5% blood
- 491 (85%) were CTX-M producers
- Compared to uninfected controls, unique predictors of CTX-M producing *E. coli* included
  - Prior UTI
  - Nursing home status/impaired functional status
  - Cephalosporin exposure

Hayakawa et al, 2012

### Unintended Consequences of Carbapenem Use

Table 1.—Change in Parenteral Cephalosporin and Imipenem/Cilastatin Use From 1995 to 1996 Following Cephalosporin Restriction in 1996

Antibiotics	Year	Unpaired Median Monthly Gram Use (Range)	Change, %	P	Paired Median Monthly Gram Use (Range)	P
All cephalosporins	1995	5558 (4452 to 8558)	-80.1	<.001	-4709 (-7168 to -3208)	<.001
	1996	1105 (259 to 1950)				
Imipenem	1995	197 (76 to 483)	140.6	<.05	258 (-140 to 551)	.05
	1996	474 (119 to 827)				

Table 4.—Change in Number and Incidence of Patient-Related Imipenem-Resistant *Pseudomonas aeruginosa* From 1995 to 1996 Following Cephalosporin Restriction in 1996

Site	Year	No. of PIR-IMP	Change, %	Incidence by Unpaired Median PIR-IMP/ADC* Ratio (Range)	P	Incidence by Paired Median Monthly PIR-IMP/ADC Ratio Difference (Range)	P
Hospital-wide	1995	67	68.7	0.015 (0.003-0.026)	<.01	0.010 (-0.008-0.031)	<.01
	1996	113					

Rahal, *JAMA*, 1998, 1233-37

### Carbapenem Resistance

- Emerging problem in *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, Enterobacteriaceae (CRE)
- Risk factors include ICU stay, prolonged exposures to healthcare, indwelling devices, antibiotic exposures
  - Long-term acute care centers (LTACs)
- Severely limits treatment options
  - Increased use of older, toxic agents such as colistin

### *Klebsiella pneumoniae* Carbapenemases (KPCs)

- Plasmid-mediated carbapenemase
- KPC-producing strains of *Klebsiella pneumoniae* and other enterobacteriaceae
  - KPC-2, KPC-3
- Endemicity in many locales in the US
  - Hyperendemicity in NYC
  - 24% of *K. pneumoniae* infections were due to KPCs in 2 hospitals
- Country-wide outbreak ongoing in Israel, Greece, Columbia and others

\*Bratu, *AAC*, 2005; Quale, *CID*, 2004; Leavitt, *AAC*, 2007; Carmeli, *Clin Micro Infect*, 2010

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### KPCs (cont)

- Might appear susceptible to imipenem or meropenem, but with borderline MICs per 2009 CLSI breakpoints
  - Usually ertapenem resistant
  - Modified Hodge test
- Usually only susceptible to colistin, tigecycline and select aminoglycosides
- Easily spread in hospitals (often requires cohorting of staff and patients to control)

### KPCs in the United States

http://www.cdc.gov/getsmart/healthcare/learn-from-others/factsheets/resistance.html

### International dissemination of *Klebsiella pneumoniae* carbapenemase (KPC)-producing Enterobacteriaceae.

Gupta N et al. Clin Infect Dis. 2011;53:60-67  
Published by Oxford University Press on behalf of the Infectious Diseases Society of America 2011. Clinical Infectious Diseases

### Outbreak of Colistin-Resistant, Carbapenem-Resistant *Klebsiella pneumoniae* in Metropolitan Detroit, Michigan<sup>7</sup>

Involved 1 LTAC, 2 hospitals  
Marchaim, Antimicrob Agents Chemother, 2011, 593-9

### New Delhi metallo-beta-lactamase-1 (NDM-1)

- Carbapenemase mediating broad spectrum resistance
  - Usually found in *Klebsiella pneumoniae*, *E. coli*
- Initially identified in India, Pakistan, Bangladesh
- Recovered in Australia, France, Japan, Kenya, North America, Singapore, Taiwan, and the United Kingdom, Australia, Canada
- Recovered in the US (Massachusetts, Illinois and California)

### *Acinetobacter baumannii*

- Traditionally ICU organism
- Now being seen in general hospital population and nursing homes
- Antimicrobial resistance is a major concern

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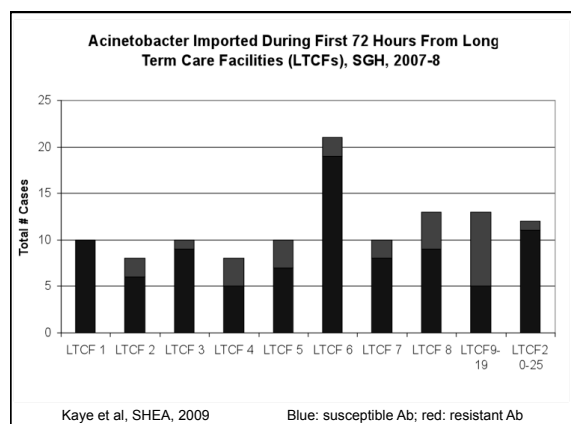
Susceptibility trends of *Acinetobacter baumannii* at Detroit Medical Center (DMC), 2003-2008\*

	No. of Isolates	Imi	A/S	Ceftaz	Cirpo	Tmp/Smx	Amik	Tobra
2003	566	99%	89%	36%	32%	33%	90%	41%
2004	593	97%	86%	43%	31%	31%	77%	36%
2005	890	99%	87%	28%	24%	26%	81%	28%
2006	751	99%	62%	26%	24%	27%	92%	56%
2007	1175	65%	37%	16%	14%	17%	63%	60%
2008	1239	42%	40%	15%	15%	18%	33%	65%

Reddy, AAC, 2009

- ### MDR GNB in Long Term Care
- Quinolone resistance increasingly common in hospitals, long-term care and in some community settings
  - B-lactam resistance established in hospitals, many long-term care settings
  - Risk factors in long-term care for resistant Gram-negative bacilli
    - Indwelling devices
    - Poor functional status
    - Pressure ulcers/wounds
    - Antimicrobial/quinolone exposure
    - Prior hospitalization

- ### Evolution of Nursing Home Care
- Long stay ⇔ short + long stay
  - Low level care ⇔ increasing acuity (long-term acute care [LTAC])
  - Wider range of residents:
    - Post-operative care
    - Rehabilitation
    - Prolonged antibiotics
    - Long-term ventilation
    - Long-term care

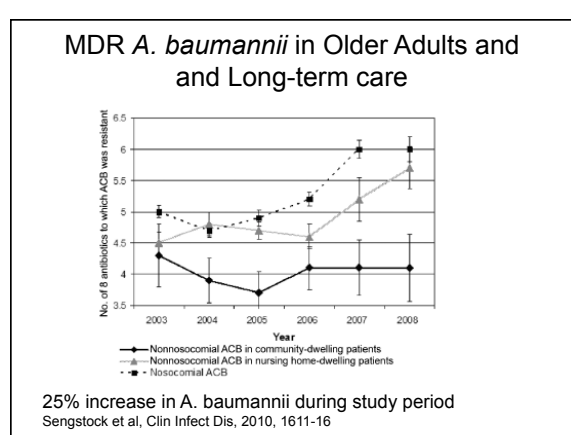


### Role of Long-term Care Facilities and MDR-GNB

Table 3  
Associations among admissions sources, health care exposures, and episodes of multidrug-resistant organisms present on admission, southeast Michigan, 2009

Organism	Direct admission source (all cohort, N = 7,147)				Exposures in past 6 months (health care systems 1 and 3 only, n = 4,805)		
	No.	LTAC	Non-LTAC LTCF	Home	No.	LTAC exposure	Hemodialysis exposure
MISA	2,340 (32.7)	18 (0.8)	282 (12.1)	2,004 (86.0)	1,719 (35.8)	15 (0.9)	38 (2.7)
MISA	1,534 (21.5)	18 (1.2)	300 (19.7)	1,183 (77.8)	820 (17.1)	31 (3.8)	26 (7.5)
VRE	654 (9.1)	26 (4.0)	288 (44.1)	320 (49.0)	416 (8.6)	47 (11.3)	24 (5.8)
Total MDR-GNO	4,528 (63.4)	62 (1.4)	870 (19.3)	3,510 (77.9)	2,951 (61.5)	93 (3.1)	88 (4.1)
ESBL	486 (6.8)	27 (5.6)	233 (47.9)	210 (43.2)	284 (5.9)	21 (7.4)	12 (4.2)
CRE	93 (1.3)	17 (18.3)	42 (45.2)	34 (36.6)	76 (11.6)	24 (31.6)	2 (4.5)
<i>A. baumannii</i>	411 (5.75)	40 (9.8)	131 (32.0)	221 (53.9)	289 (6)	43 (14.9)	16 (5.6)
<i>P. aeruginosa</i>	1,629 (22.8)	64 (3.9)	316 (19.4)	1,198 (73.6)	1,201 (25)	70 (5.8)	32 (2.7)
Total MDR-GNO	2,619 (36.6)	148 (5.7)	722 (27.6)	1,663 (63.6)	1,850 (38.5)	158 (8.5)	62 (3.4)

Admission from LTAC increased risk for MDR-GNR > 3-fold  
Marchaim et al, AJIC, 2012



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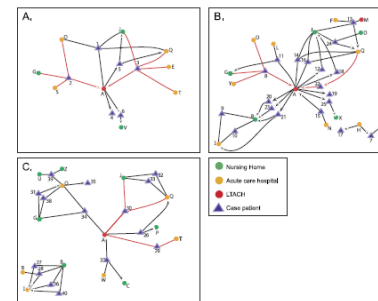
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#### Emergence and Rapid Regional Spread of *Klebsiella pneumoniae* Carbapenemase-Producing *Enterobacteriaceae*

Sarah Y. Won,<sup>1,2</sup> L. Silvia Munoz-Price,<sup>3</sup> Karen Lolans,<sup>4</sup> Bala Hota,<sup>4,5</sup> Robert A. Weinstein,<sup>4,6</sup> and Mary K. Hayden<sup>1</sup> for the Centers for Disease Control and Prevention Epicenter Program

<sup>1</sup>Hunter Holmes McGuire Veterans Affairs Medical Center, and <sup>2</sup>Virginia Commonwealth University, Division of Infectious Diseases, Richmond, Virginia; <sup>3</sup>Department of Medicine and Department of Public Health and Epidemiology, University of Miami Miller School of Medicine, Florida; <sup>4</sup>Rush University Medical Center, Chicago, Illinois; and <sup>5</sup>Department of Medicine, Cook County Health and Hospital Systems, Chicago, Illinois



**Figure 3.** Exposure network graphs delineating the relationships of cases to long-term acute care hospitals (LTACHs), acute care hospitals, and nursing homes during 3 epidemiologic periods. Case patients and facilities to which case patients were linked are connected by arrows or by nondirectional lines.

#### Strategies to Control the Spread of MDR GNB

- Contact precautions/hand hygiene
- Environment and source control
- Antibiotic stewardship
- Enhanced infection control measures
- Bundles

#### Barrier Precautions: Do They Work to Limit the Spread of Multi-Drug Resistant Organisms?

- In outbreak settings, gowns/gloves effective in preventing spread of multidrug-resistant organisms (MDROs)
- In terms of prevention of endemic spread, data are mostly observational
- Success with many different types of MDROs
  - *Clostridium difficile*
  - Methicillin-resistant *S. aureus* (MRSA)
  - Vancomycin-resistant enterococcus (VRE)
  - MDR Gram-negatives (including carbapenem-resistant enterobacteriaceae (CRE), extended-spectrum B-lactamase-producers (ESBLs), *Acinetobacter baumannii*)

Anderson, Infect Dis Clin N Am 23 (2009) 847–864

Frequency of Contamination of Gowns, Gloves, and Hands of Healthcare Workers (HCWs) after Caring for Patients Colonized or Infected with Specified Bacteria

Source of culture-positive sample	No. (% [95% CI]) of observations	
	Patients with MDR <i>Acinetobacter baumannii</i> carriage (n = 199)	Patients with MDR <i>Pseudomonas aeruginosa</i> carriage (n = 134)
Gloves	72 (36.2 [29.5–42.9])	9 (6.7 [2.5–11.0])
Gown	22 (11.1 [6.7–15.4])	6 (4.5 [1.0–8.0])
Gloves and/or gown	77 (38.7 [31.9–45.5])	11 (8.2 [3.6–12.9])
Hands <sup>a</sup>	9 (4.5 [1.6–7.4])	1 (0.7 [0–2.2])

Morgan, Infect Control Hosp Epi, 2010, 716-21

#### Role of the Environment

- Environmental sources of contamination/infection
  - Increasingly recognized as sources of infection
- Particularly important with pathogens such as *Clostridium difficile*, Norovirus, *Acinetobacter* spp.
- Bleach preparations are more effective for some pathogens (still need cleaning)
- Latest technology being tested: UV light, hydrogen peroxide vapor

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#### Environmental cleaning

- Adequacy of cleaning of patients' rooms suboptimal
- Improve monitoring and feedback of efficacy of cleaning
  - Direct observation and culturing not efficient, time-consuming and expensive
- Other options: ATP bioluminescence and fluorescent dyes
  - Monitor process, efficacy of cleaning

#### Supplements to Routine Environmental Cleaning

- Disinfection units that decontaminate environmental surfaces
- Must remove debris and dirt in order for these units to be effective
- Two most common methods
  - UV light
  - Hydrogen peroxide (HP)

#### Are Room Decontamination Units Needed to Prevent Transmission of Environmental Pathogens?

William A. Rutala, PhD, MPH<sup>1</sup> David J. Weber, MD, MPH<sup>1</sup>

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY AUGUST 2011, VOL. 32, NO. 8

TABLE 1. Comparison of Room Decontamination Systems That Use UV Irradiation and Hydrogen Peroxide (HP)

	Sterinis	Steris	Bioquell	Tru-D
Abbreviation	DMHP (dry mist HP)	VHP (vaporized HP)	HPV (HP vapor)	UV-C
Active agent	Stemal (5% HP, <50 ppm silver cations)	Vaprox (35% HP)	35% HP	UV-C irradiation at 254 nm
Application	Aerosol of active solution	Vapor, noncondensing	Vapor, condensing	UV irradiation, direct and reflected
Aeration (removal of active agent from enclosure)	Passive decomposition	Active catalytic conversion	Active catalytic conversion	Not necessary
Sporicidal efficacy	Single cycle does not inactivate <i>Bacillus anthracis</i> BIs; ~4-log <sub>10</sub> reduction in <i>Clostridium difficile</i> and incomplete inactivation in situ	Inactivation of <i>Grobacillus stearothermophilus</i> BIs	Inactivation of <i>G. stearothermophilus</i> BIs; ~6-log <sub>10</sub> reduction in <i>C. difficile</i> in vitro and complete inactivation in situ	1.7–4-log <sub>10</sub> reduction in <i>C. difficile</i> in situ
Evidence of clinical impact	None published	None published	Significant reduction in the incidence of <i>C. difficile</i>	None published

NOTE. Adapted from Otter and Yezli.<sup>18</sup> BIs, biological indicators; VRE, vancomycin-resistant *Enterococcus*.  
<sup>1</sup> All *C. difficile* experiments were done with *C. difficile* spores.

#### Room Decontamination Systems: Pros and Cons

- Advantages
  - Effective in eliminating vegetative bacteria
  - Sporicidal (HP > UV light)
- Disadvantages
  - Capital cost
  - Room turnover
  - Does not obviate cleaning

#### Chlorhexidine Gluconate (CHG)

- Broad-spectrum antimicrobial disinfectant
- Preferred agent for skin preparation prior to insertion of vascular catheter and prior to surgery
- Studied for “source control”, decrease in degree of contamination of patients by problem hospital pathogens

#### Prevention of Bloodstream Infections by Use of Daily Chlorhexidine Baths for Patients at a Long-Term Acute Care Hospital

L. Silvia Munoz-Price, MD; Bala Hota, MD, MPH; Alexander Stemer, MD; Robert A. Weinstein, MD

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY NOVEMBER 2009, VOL. 30, NO. 11

- Intervention in LTAC consisted of daily CHG bathing of patients
- 99% reduction in CLABSI by end of intervention period

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TABLE 1. Organisms Isolated in Culture of Samples From Patients with Central Venous Catheter-Associated Bloodstream Infection, by Study Period

Variable	Preintervention period (n = 59)	Intervention period (n = 29)	Postintervention period (n = 51)
<b>Pathogen</b>			
CNS	30 (51)	11 (38)	20 (39)
<i>Enterococcus</i>	12 (20)	5 (17)	12 (24)
<i>Candida</i>	9 (15)	6 (21)	3 (6)
<i>Acinetobacter</i>	8 (13)	2 (7)	6 (12)
<i>Pseudomonas</i>	4 (7)	1 (3)	10 (12)
<i>Enterobacter</i>	4 (7)	0 (0)	2 (4)
<i>Corynebacterium</i>	3 (5)	0 (0)	0 (0)
LF GNR	3 (5)	4 (14)	8 (16)
MRSA	0 (0)	1 (3)	7 (14)
Other	2 (3)	0 (0)	0 (0)
<b>No. of pathogens<sup>a</sup></b>			
1 pathogen	44 (75)	28 (97)	36 (70)
2 pathogens	14 (23)	1 (3)	10 (20)
3 pathogens	1 (2)	0 (0)	5 (10)

NOTE. Data are no. (%) of isolates. CNS, coagulase-negative *Staphylococcus*; LF GNR, lactose fermentor gram-negative rod; MRSA, methicillin-resistant *Staphylococcus aureus*. For descriptions of the 3 different study periods and their interventions, see Methods.  
<sup>a</sup> Per blood culture set.

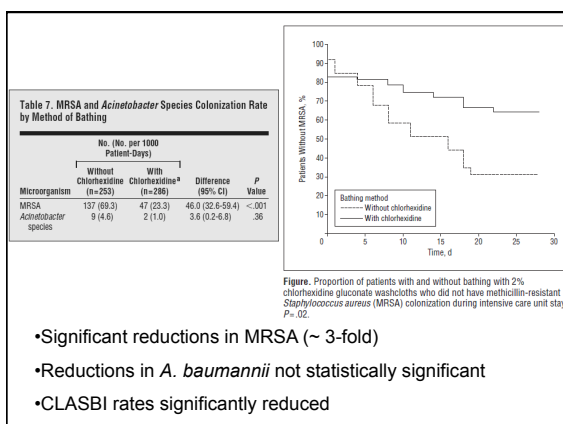
### Effect of Chlorhexidine Whole-Body Bathing on Hospital-Acquired Infections Among Trauma Patients

Heather L. Evans, MD, MS; Timothy H. Dellit, MD; Jeannie Chan, PharmD, MS; Avery B. Nathens, MD, PhD; Ronald V. Maier, MD; Joseph Cuschieri, MD

*Arch Surg.* 2010;145(3):240-246

Observational study, pre/post implementation of CHG cloth bathing in trauma ICU

Main outcomes: VAP, CLABSI and colonization with MDROs



### Antimicrobial Stewardship - Goals

- Optimize appropriate use of antimicrobials
  - The right agent, dose, timing, duration, route
- Optimize clinical outcomes
  - Reduce emergence of resistance
  - Limit drug-related adverse events
  - Minimize risk of unintentional consequences
- Help reduce antimicrobial resistance
  - The combination of effective antimicrobial stewardship and infection control has been shown to limit the emergence and transmission of antimicrobial-resistant bacteria

Dellit TH et al. *Clin Infect Dis.* 2007;44(2):159–177; . Drew RH. *J Manag Care Pharm.* 2009;15(2 Suppl):S18–S23; Drew RH et al. *Pharmacotherapy.* 2009;29(5):593–607.

### Enhanced Infection Control Processes

- Active Surveillance
  - Use of “screening” cultures to identify patients colonized with pathogens (usually MDR) of interest
  - Goal is to prevent spread in the hospital by identifying patients who are colonized and intervening to prevent spread
  - Most experience is with Gram positive pathogens
  - Limited use for some pathogens (due to low sensitivity)
- Cohorting of patients
- Dedicated staff

### Bundles

- A bundle is a structured way of improving the processes of care and patient outcomes: a small, straightforward set of evidence-based practices (e.g. 3-5) that, when performed collectively and reliably, have been proven to improve patient outcomes.

Resar R. *Joint Commission Journal on Quality and Patient Safety.* 2005; 243-248



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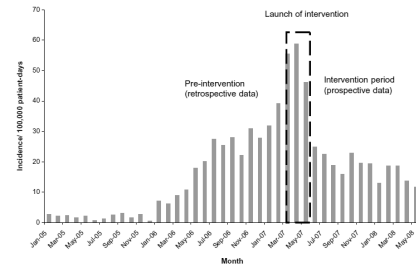
#### Containment of a Country-wide Outbreak of Carbapenem-Resistant *Klebsiella pneumoniae* in Israeli Hospitals via a Nationally Implemented Intervention

Mitchell J. Schwaber,<sup>1</sup> Boaz Lev,<sup>2</sup> Avi Israeli,<sup>2</sup> Ester Soltes,<sup>1</sup> Gill Smolian,<sup>1</sup> Bina Rubinovitch,<sup>1</sup> Itamar Shalit,<sup>1</sup> Yehuda Carmeli,<sup>1</sup> and the Israel Carbapenem-Resistant Enterobacteriaceae Working Group<sup>3</sup>

<sup>1</sup>National Center for Infection Control, Israel Ministry of Health, Tel Aviv, and <sup>2</sup>Israel Ministry of Health, Jerusalem, Israel

CID 2011;52 (1 April) • Schwaber et al

- Country-wide outbreak of KPCs
- Coordinated taskforce
- Intervention consisted of
  - Active surveillance screening for KPC carriage
  - Contact precautions
  - Cohorting of staff and patients



**Figure 1.** Monthly incidence of carbapenem-resistant Enterobacteriaceae detected by clinical culture per 100,000 patient-days, January 2005–May 2008. The intervention was gradually implemented nationwide from March through May 2007. Data through May 2007 were assembled retrospectively, data from 1 June 2007 through 31 May 2008 were collected prospectively. The intervention led to a reduction in monthly incidence from pre-intervention peak of 55.5 cases per 100,000 patient-days in March 2007 to 11.7 cases per 100,000 patient-days in May 2008 ( $P < .001$ ).

#### An APIC Guide to the Elimination of Multidrug-resistant *Acinetobacter baumannii* Transmission in Healthcare Settings (2010)

- Extensive summary of strategies
- Stresses important of surveillance, understanding local epidemiology and adherence to infection control practices
- Active surveillance/screening cultures of limited value
  - 55% sensitivity

#### A Multifaceted Intervention to Reduce Pandrug-Resistant *Acinetobacter baumannii* Colonization and Infection in 3 Intensive Care Units in a Thai Tertiary Care Center: A 3-Year Study

Anucha Apisarnthanarak,<sup>1</sup> Uayporn Pinitcheai,<sup>1</sup> Kanokporns Thongthabtheth,<sup>1</sup> Chansawat Yonkyun,<sup>1</sup> David K. Warren,<sup>2</sup> and Victoria J. Fraser,<sup>2</sup> for the Thammasat University Pandrug-Resistant *Acinetobacter baumannii* Control Group

<sup>1</sup>Division of Infectious Diseases and Infection Control and <sup>2</sup>Medical Intensive Care Unit, Thammasat University Hospital, Pathumthani, Thailand, and <sup>3</sup>Division of Infectious Diseases, Washington University School of Medicine, St. Louis, Missouri

Clinical Infectious Diseases 2008;47:760–7

- Multifaceted intervention to decrease the incidence of MDR *A. baumannii*
- Enhanced infection control precautions
- Active surveillance (tracheal aspirates, rectal swab)
- Cohorting of infected/colonized patients<sup>46</sup>
- Bleach environmental cleaning

**Table 3.** Rate of pandrug-resistant *Acinetobacter baumannii* infection and colonization among intervention intensive care units.

Unit	No. of cases per 1000 patient-days		
	Period 1	Period 2	Period 3
Medical intensive care	1.4	0.5 <sup>a</sup>	0.4 <sup>a</sup>
Surgical intensive care	1.2	0.45 <sup>a</sup>	0.25 <sup>a</sup>
Coronary care	1.0	0.25 <sup>a</sup>	0.2 <sup>a</sup>

**NOTE.** Period 1 was the baseline period (1 January 2005 through 31 December 2005). Period 2 was the intervention period (1 January 2006 through 31 December 2006). Period 3 was the follow-up period (1 January 2007 through 31 December 2007).

<sup>a</sup>  $P < .05$ , compared with period 1.

#### Conclusions

- MDR GNB are growing in prevalence in multiple geographic locales
- Occur in a variety of healthcare associated settings
  - Even in the community
- Antimicrobial stewardship is here to stay
- Problem is compounded by dry pharmaceutical pipeline
- Novel methods to control spread of MDROs are attractive but not clearly effective/cost-effective

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**Infections due to Multi-Drug Resistant (MDR) Gram-Negative Pathogens**  
**Prof. Keith Kaye, Wayne State University**  
**Broadcast live from the 2012 APIC conference ([www.apic.org](http://www.apic.org))**

**Conclusions (2)**

- Technologic advances regarding environmental hygiene are helpful
- Technology and protocols alone will not prevent infections – need compliance with basic process components
- No single process is completely effective in limiting the spread of MDR GNB
  - Bundled interventions have been successful
- Regional approaches to controlling the spread of antimicrobial resistance are needed
  - Increased CDC and public health involvement