

The Emergence of *Acinetobacter* as a Hospital Pathogen

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Outline

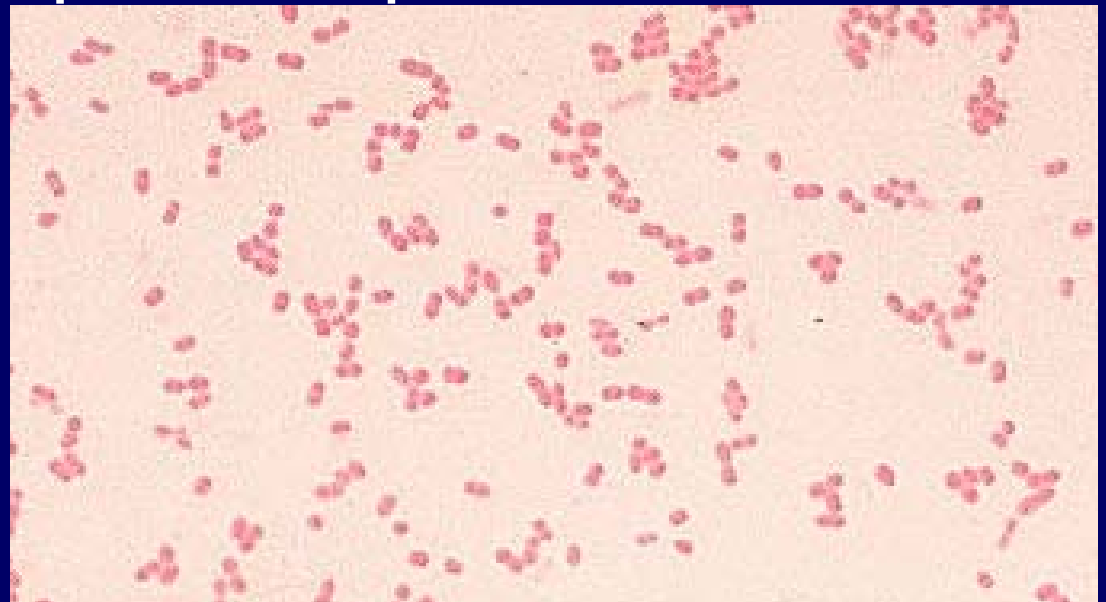
- What is *Acinetobacter*?
- Where is it found?
- Who does it infect?
- Why is it so successful as a healthcare associated pathogen?
- How can we prevent and treat *Acinetobacter* infections?

Acinetobacter

- Greek for nonmotile rod (Akinetos)
- Aerobic, oxidase-negative nonfermenter
- Non reactive on many biochemical tests
- 25 genospecies, but *A. baumannii* most common and important species

Gram negative
coccobacilli

Brisou and Prévot, 1954



Acinetobacter. Where is it found?

- Widely distributed in nature (soil, water)
- More common in hot, humid climates
- Primarily a pathogen of hospitals
 - Can colonize skin, wounds, resp/GI tracts
- More recent emergence as hospital pathogen in temperate climates
- Seasonal variation
 - 50% increase in infection rates from July-Oct

Munoz-Price and Weinstein. N Engl J Med 2008;12:1271-81.
McDonald LC, et al. Clin Infect Dis 1999;29:1133-7.

Who gets *Acinetobacter* Infections?

- Risk factors:
 - Advanced age
 - [Prolonged] ICU stay
 - Surgery
 - Use of antimicrobial agents
 - 3rd Ceph, FQ, carbapenems
 - Invasive device use (CVC)
 - Mechanical ventilation

Villegas et al. Infect Control Hosp Epidemiol 2003;24:284.

Manikal et al. Clin Infect Dis 2000;31:101.

Garnacho-Montero, et al. Intensive Care Med 2005;31:649.

Acinetobacter: Who Does it infect?

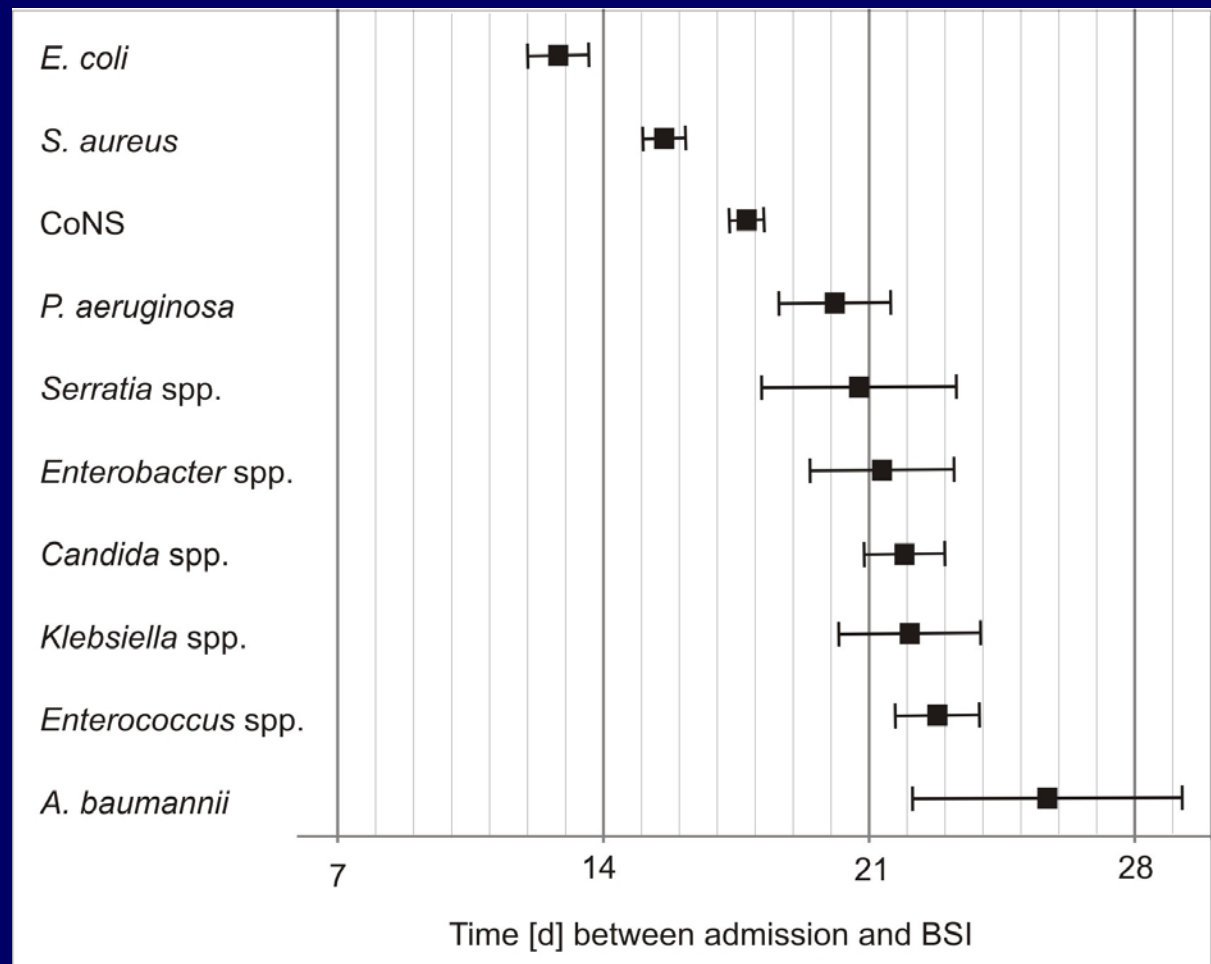
NHSN Data, Jan '06-Oct '07

Infection site	Rank	% of infections
VAP	3	8.4
CLA-BSI	9	2.2
CA-UTI	9	1.2
SSI	9	0.6

463 U.S. Hospitals in the National Healthcare Safety Network
Hidron AI, et al. Infect Cont Hosp Epidemiol 2008;29:996-1011.

Acinetobacter BSI

- SCOPE study
- 0.6/10K admits
- 1.6% of ICU BSI
- Crude mortality
 - 34% overall
 - 43% in ICU
- Later onset



Wisplinghoff H, et al. Clin Infect Dis. 2004;39:309-17

Impact of Nosocomial *Acinetobacter* infection

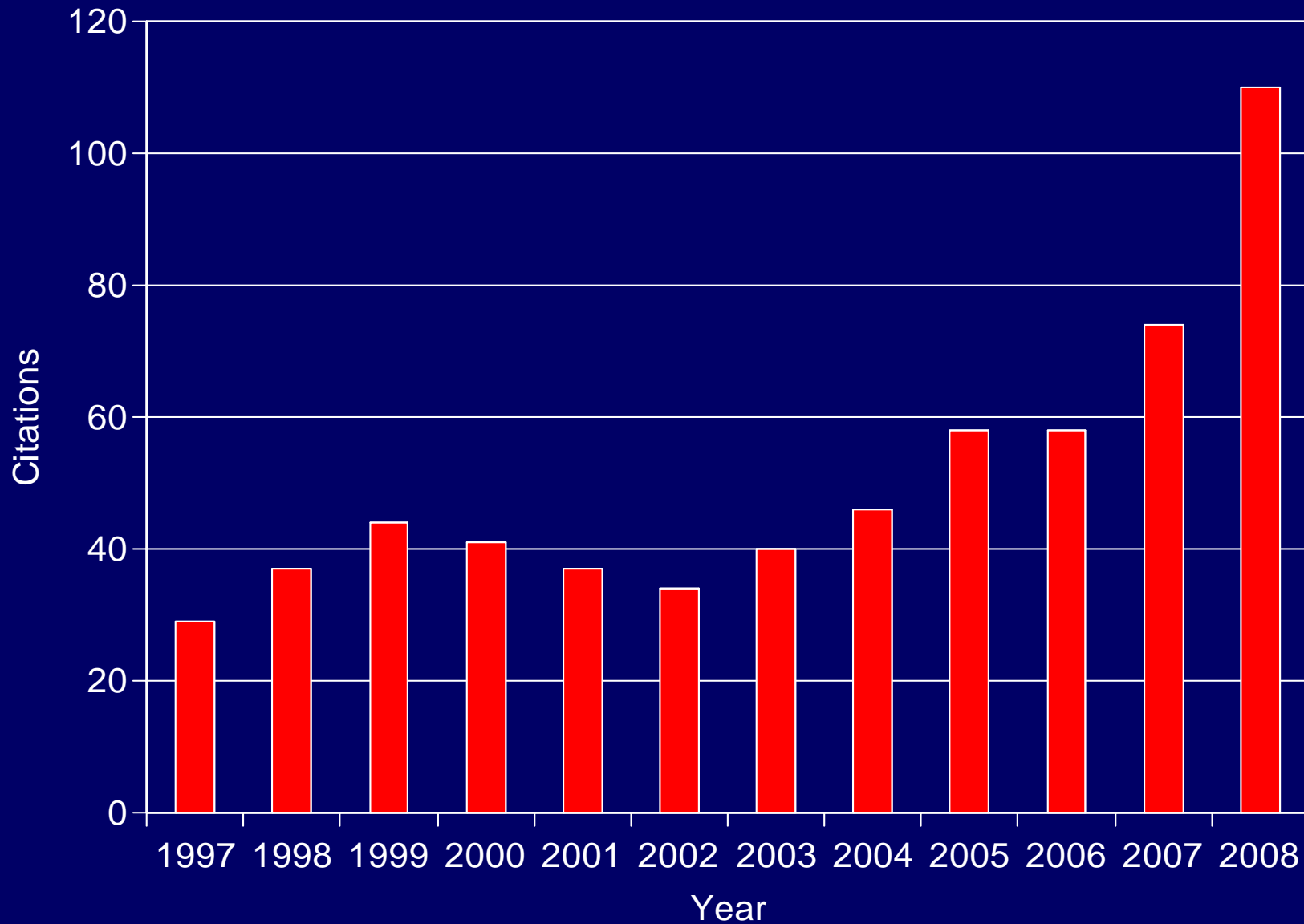
Infection	Mortality		Difference
	Cases	Controls	
BSI ¹	42%	34%	8%
VAP ²	40%	28%	12%
VAP ³	70%	17%	53%
Any ³	58%	15%	43%

1. Blot S et al. Intensive Care Med 2003;29:471.

2. Garnacho et al. Crit Care Med 2003;10:2478.

3. Garcia-Garmendia et al. Crit Care Med 1999;27:1794.

PubMed Citations for “Nosocomial Acinetobacter”



Acinetobacter: Why so successful?

NHSN Data, Jan '06-Oct '07

Infection site	N tested	% R to carbapenems
VAP	498	36.8
CLA-BSI	219	29.2
CA-UTI	82	25.6
SSI	36	30.1

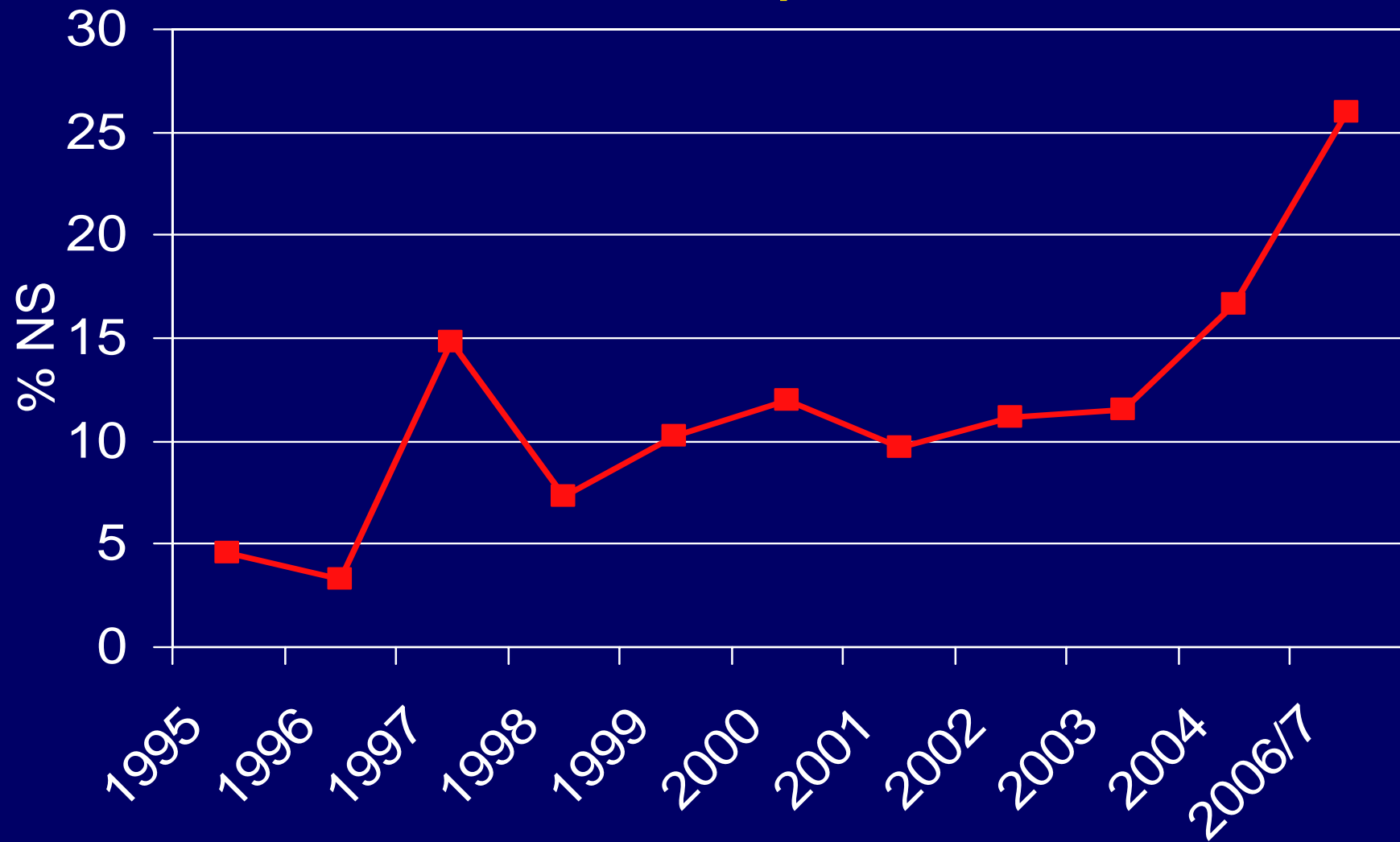
463 U.S. Hospitals in the National Healthcare Safety Network
Hidron AI, et al. Infect Cont Hosp Epidemiol 2008;29:996-1011.

CDC definition of MDR *Acinetobacter*

- Resistant to all tested agents in ≥ 3 of the “commonly prescribed” classes:
 - Beta-lactams (including aztreonam)
 - Quinolones
 - Aminoglycosides
 - Carbapenems

Arjun Srinivasan, MD, CDC.

MDR-Acinetobacter NNIS/NHSN Hospitals 1995-2007



Arjun Srinivasan, MD, CDC.

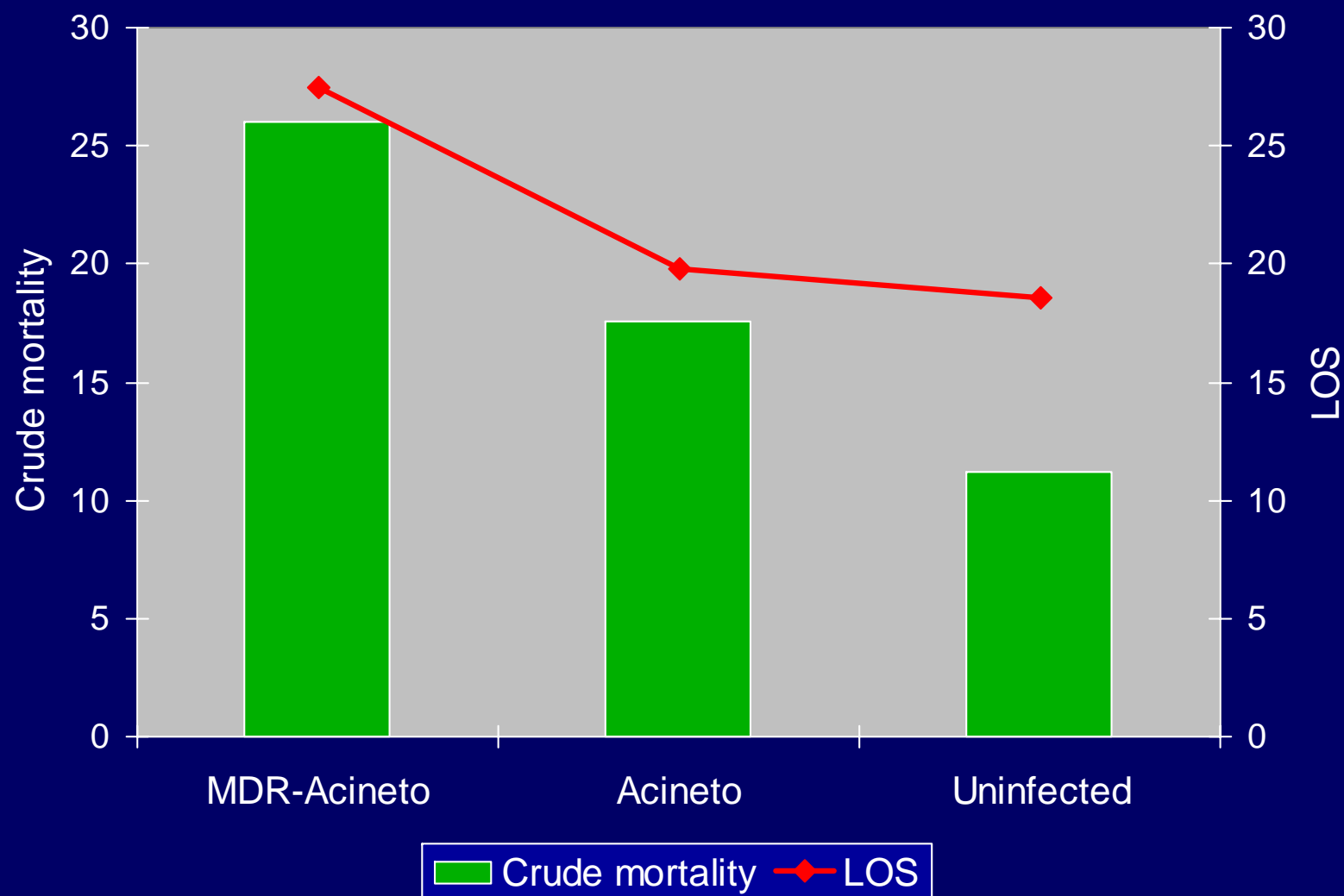
Acinetobacter.

Mechanisms of Resistance

- **Beta-lactamases**
 - ESBL (acquired, mobile genetic elements)
 - Serine and metallo-beta lactamases
 - AmpC (chromosomal cephalosporinases)
- **Alterations in cell wall channels (porins)**
- **Efflux pumps (multiple abx classes)**
- **Other classes (FQ, AG, etc.)**
- Resistance island recently reported, containing 45 resistance genes

Fournier PE, et al. PLoS Genet 2006;2:e7.

Acinetobacter: Impact of MDR?



N = 96, 91, 89 Sunenshine et al. Emerg Infect Dis 2007;13:97-103.

Acinetobacter: Why so successful?

Transmission in the Hospital Setting

- Direct or indirect contact
 - Contaminated hands of healthcare workers
- Airborne transmission via aerosol production (e.g., hydrotherapy) or from patients with respiratory colonization or infection

Simor AE et al. Infect Control Hosp Epidemiol 2002;23:261-267.

Surveillance for MDR *A. baumannii*

- 52 patients with carriage (recent or remote) were sampled at 6 body sites
- Sensitivity only 55% for recent carriers
 - Pharynx, wounds, ET aspirates highest yield
- 5/30 remote carriers were +, mean duration of 17.5 months, up to 42 months
- Bottom line: Carriage of MDR *A. baumannii* can be prolonged, and even multisite sampling may be insensitive

Marchaim et al. J Clin Microbiol 2007;45:1551.

Acinetobacter Colonization in a Non-outbreak Setting

- Active surveillance cultures for MDR *Acinetobacter* on 1111 consecutive patients admitted to adult ICU.
- Sites: axilla, wounds, respiratory
- Frequency: admission and weekly
- Admission prevalence: 0.82%
- Possible Transmission rate: 0.43%
- LTCF exposure: RR 19 [6.6-54]

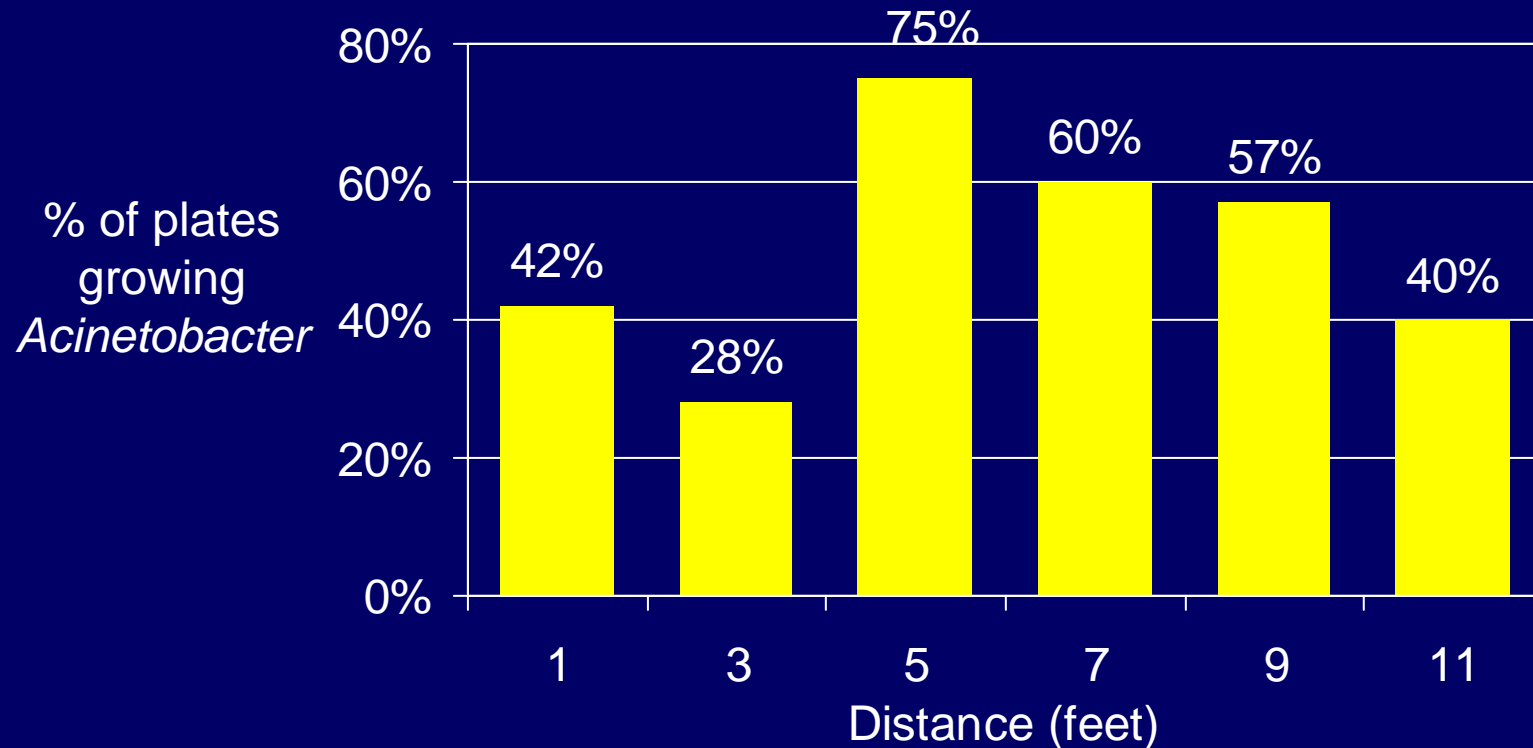
Maragakis et al. JAMA 2008;299:2513.

Acinetobacter Surveillance in a Long-Term Acute Care Unit

- Long term acute care (LTAC) units and hospitals are a fast-growing segment of healthcare
- Active surveillance for *A. baumannii* at one LTAC (nares, perirectal, sputum, wound):
 - 44/147 (30%) patients were colonized

Evidence for Airborne Transmission of *Acinetobacter*

- Sedimentation plates placed in 7 patients' rooms with respiratory infection or colonization



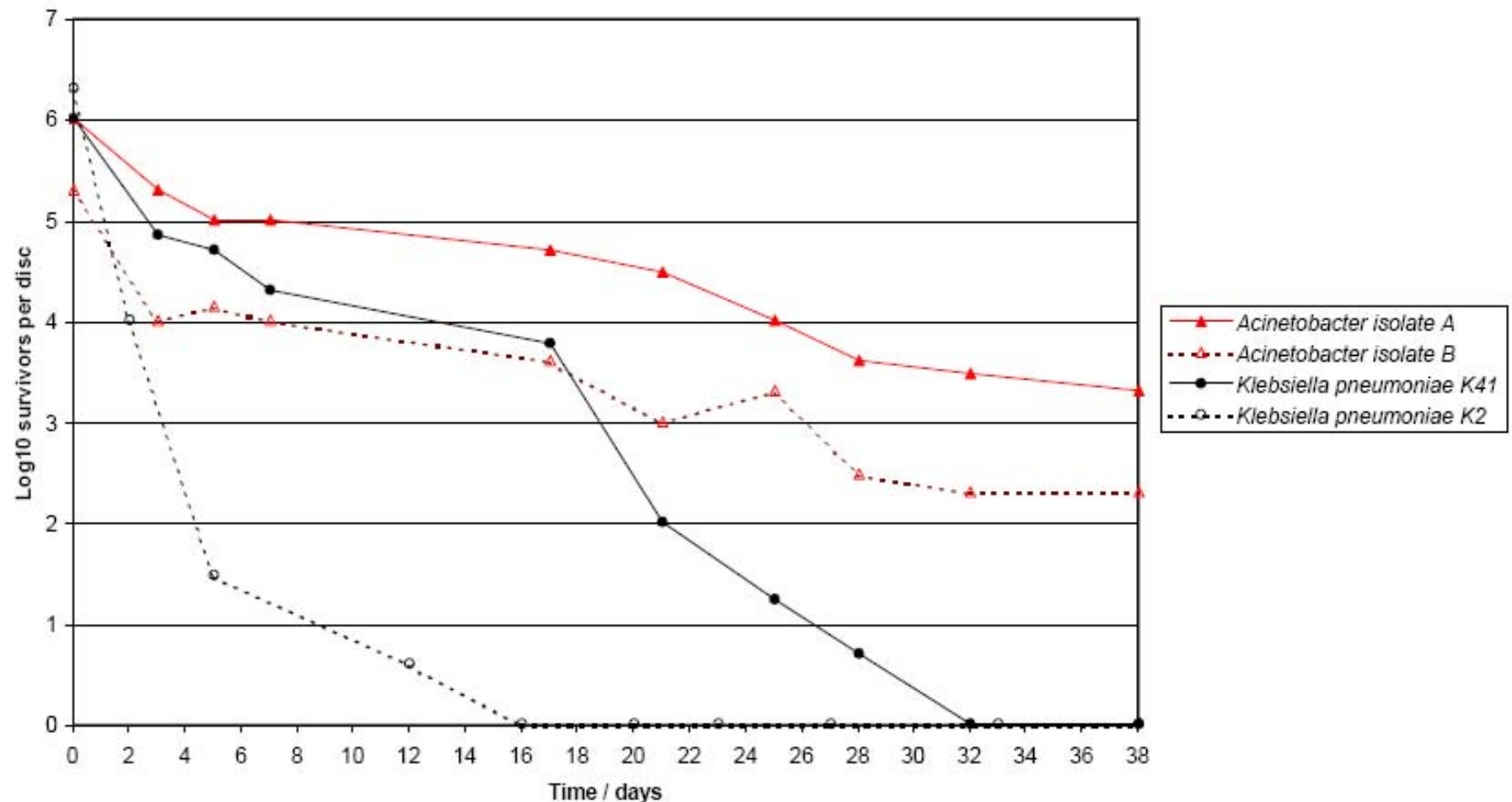
Brooks SE et al. Infect Control Hosp Epidemiol 2000;21:304.

Environmental Contamination with *Acinetobacter*

- Bed rails
- Bedside tables
- Ventilators
- Infusion pumps
- Mattresses
- Pillows
- Air humidifiers
- Patient monitors
- X-ray view boxes
- Curtain rails
- Curtains
- Equipment carts
- Sinks
- Ventilator circuits
- Floor mops
- Keyboards

Environmental Survival of Gram Negatives

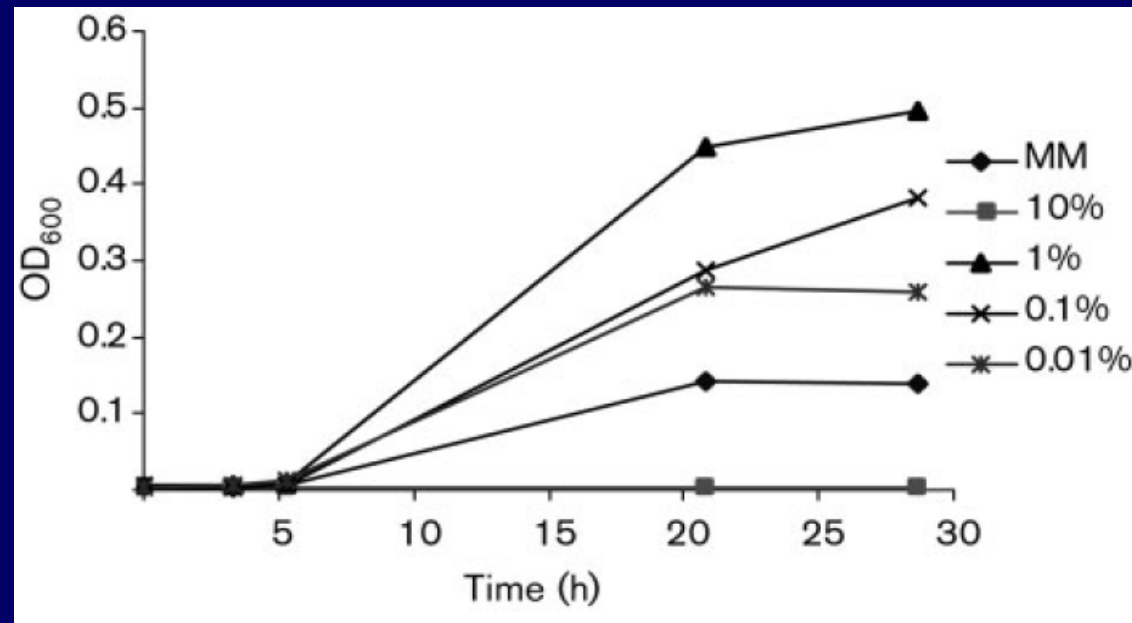
Survival of clinical isolates dried onto stainless steel discs in room air



Acinetobacter and EtOH:

Antimicrobial or growth promoter?

- Low concentrations of alcohol hand rubs (<1%) enhanced growth of Acinetobacter
- Also ↑ OmpA secretion, which may confer increased pathogenicity



Edwards J, et al. J Med Microbiol 2007;56:1595-99.

Acinetobacter Colonization of Healthcare Workers

- Outbreak of multidrug resistant *A. baumannii* in a Dutch ICU (66 patients)
- Nursing staff were cultured (nares & axilla)
 - 15 nurses carried epidemic strain
 - All were culture negative when re-cultured (nose, throat, axilla, perineum)
- Gram negatives, including *Acinetobacter*, often found as transient flora on HCW hands

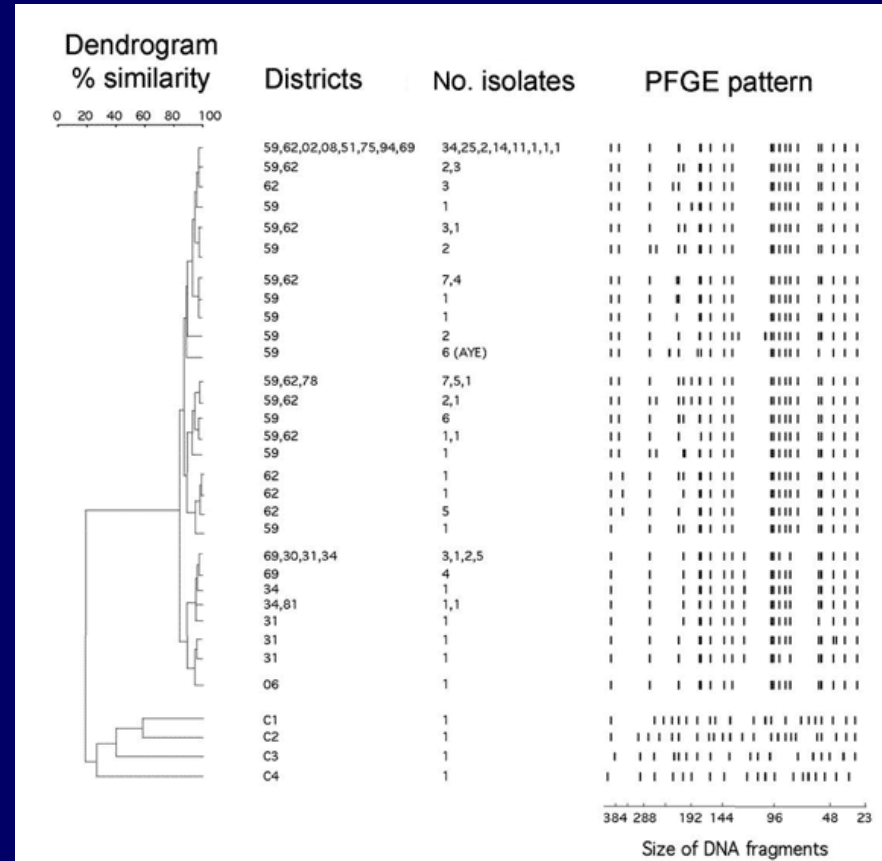
Wagenvoort JHT et al. Eur J Clin Microbiol Infect Dis 2002;21:326-327.
Bauer TM, et al. J Hosp Infect 1990;15:301-309.

Factors Promoting Transmission of *Acinetobacter* in the ICU

- Long survival time on inanimate surfaces
 - 11 days survival on Formica, 12 days on stainless steel
Webster C et al. Infect Control Hosp Epidemiol 2000;21:246.
 - Up to 4 months on dry surfaces
Wendt C et al. J Clin Microbiol 1997;35:1394-1397
- Extensive environmental contamination
- Large number of colonized patients
- Frequent contamination of the hands of HCWs
- Highly antibiotic resistant

Acinetobacter Outbreaks

- Reports increasingly common
- Most have respiratory tract predominant
- Many have common source identified
 - Respiratory equipment (vent circuits, temp probes, spirometers, suction cath, peak flow meter)
- Multihospital outbreaks often described



Lolans et al. *Anitmicrob Agents Chemother* 2006;50:2941-5.

Villegas et al. Infect Control Hosp Epidemiol 2003;24;284-295.

Manikal et al. Clin Infect Dis 2000;31:101-106.

Naas et al. Emerg Infect Dis 2006;12:1214-22.



Acinetobacter baumannii Infections Among Patients at Military Medical Facilities Treating Injured U.S. Service Members, 2002--2004

- 102 soldiers with bloodstream infection
- Over 1/3 susceptible only to imipenem, some resistant to all tested agents
- Wartime infections/outbreaks not new, reports from Vietnam and Korean wars

Lindberg et al. Ann Surg 1955;141:369-74.

Tong MJ. JAMA 1972;219:1044-47.

Acinetobacter and Disaster Events

- Tsunami victims in 2004
 - 20% of wounds yielded MDR *Acinetobacter* in one referral hospital for evacuees
- Marmara earthquake, Turkey, 1999
 - *A. baumannii* most prevalent nosocomial pathogen in ICUs in which casualties treated
- Bali terrorist bombing, 2002
 - *A. baumannii* infected pt transferred to Swiss ICU, presumed source of ICU outbreak

Maegle et al. Crit Care Med 2005;33:1136.

Oncul et al. J Hosp Infect 2002;51:47.

Zanetti et al. Infect Cont Hosp Epidemiol 2007;28:723.

Acinetobacter Infections during Wars and Disasters

- Studies have identified multiple factors:
 - Skin colonization?
 - Local exposures (foods, environment)
 - Wound contamination in battlefield
 - Environmental spread and cross-transmission in field hospitals and referral hospitals

Slide adapted from Dr. Arjun Srinivasan, CDC.

How Can We Prevent *Acinetobacter* Transmission?

General Measures

- Hand hygiene
 - Use of alcohol-based hand sanitizers
 - Chlorhexidine resistance has been described
- Contact precautions
 - Gowns/gloves
 - Dedicate non-critical devices to patient room
- Environmental cleaning and disinfection
- Prudent use of antibiotics

Preventing *Acinetobacter* Transmission

Second Tier Interventions

- Point prevalence/surveillance cultures
- Focus on environmental disinfection, consider environmental cultures following terminal disinfection to document cleaning efficacy
- Cohorting
- Save all isolates for molecular typing
- Healthcare worker education
- If transmission continues, closure of unit to new admissions

Questions about Active Surveillance for *Acinetobacter*

- What's the best site?
 - Respiratory and wound sites highest yield
 - But some evidence suggests all are poorly sensitive, even when multiple sites cultured
- Who is “high-risk”?
 - Patients exposed to LTCFs
 - Other risks not as well defined
 - Reserve for outbreaks only?
- Screen for all Acineto, or just MDR?

Acinetobacter Outbreaks: More Challenging?

- Systematic review of over 1500 hospital outbreaks over 40 years
- Unit closure (usually for cleaning) required in 23% of 105 *Acinetobacter* outbreaks, versus 11.7% due to other pathogens
- Extensive and persistent environmental contamination, prolonged human carriage, multidrug resistance likely all play a role

Hansen S, et al. J Hosp Infect 2007;65;348.

Treatment of *Acinetobacter* infections

- If susceptible, carbapenems, cephalosporins, beta-lactam/beta-lactamase (sulbactam activity)
 - Alone or in combination (AG, rifampin)
- For MDR:
 - Tigecycline: resistance emerging, ? use for BSI, MDR-Acineto have occurred during tx
 - Polymyxins B and E (colistin)
 - Combination? (imipenem, rifampin, azithromycin)
 - Hetero-resistance as a rationale for combo tx

Munoz-Price LS, Weinstein R. NEJM 2008;358:1271.
Linden PK, et al. Clin Infect Dis 2006;43:S2:S89.
Urban C et al. Clin Infect Dis 2003;36:1268.

Summary (1)

- *Acinetobacter* is a growing challenge in hospital, particularly as a cause of pneumonia among sick ICU patients
- Outbreaks are common, and often involve multiple healthcare facilities
- Ability to accumulate multiple drug resistances, and to survive for prolonged periods in the environment, favor persistence and spread in healthcare setting

Summary (2)

- Preventing emergence and transmission of *Acinetobacter* in healthcare setting involves standard IC measures for MDRO control
 - HH, environmental disinfection, surveillance and contact isolation, seek common source
 - Closure of unit may be necessary
 - Antibiotic use control
- Treatment challenging, more data needed