

# ***Acinetobacter baumannii*: Just a Bad Marker of Prognosis or a Real Killer**

**Murat Akova, M.D., FESCMID, FIDSA**

**Hacettepe University School of Medicine,  
Department of Infectious Diseases,  
Ankara, Turkey**



# ***A. baumannii* is a Persistent Pathogen in the Hospital Environment**

- **No toxin or genetic determinant accountable for virulence**
- **The main virulence strategy is '*persist and resist*'**
  - **Resistance to most antibacterials**
  - **Resistance to desiccation**
    - **27 days (21 to 33 days) survival time on glass coverslips)**
  - **Resistance to disinfectants**
  - **Biofilm and motility**

**Peleg AY, et al. Clin Microbiol Rev 2008;21:538-82  
Harding CM, et al. Nature Rev Microbiol 2018;16:91**

# Surface Cleaning for Infection Control

- **MRSA**
  - Can survive a year in hospital dust
- **VRE, 4 months**
- ***C. difficile*, 5 months**
- ***A. baumannii*, 5 months**
- **The data are lacking for other MDR Gram-negative bacteria**
  - Enteric and pseudomonads may survive >1 year under certain conditions

# Transmission Dynamics of *A. baumannii* in ICU

- 5 centers in Turkey
- Prospective cohort study
- Patients admitted to the ICU and stayed at least 48 h
- 6 months surveillance, every other day in the 1<sup>st</sup> week and once a week thereafter
  - Pharyngeal, rectal and skin swabs
  - Patient beds, tables and buttons of respiratory pumps
  - Computer keyboards, telephones
  - HCW's hands

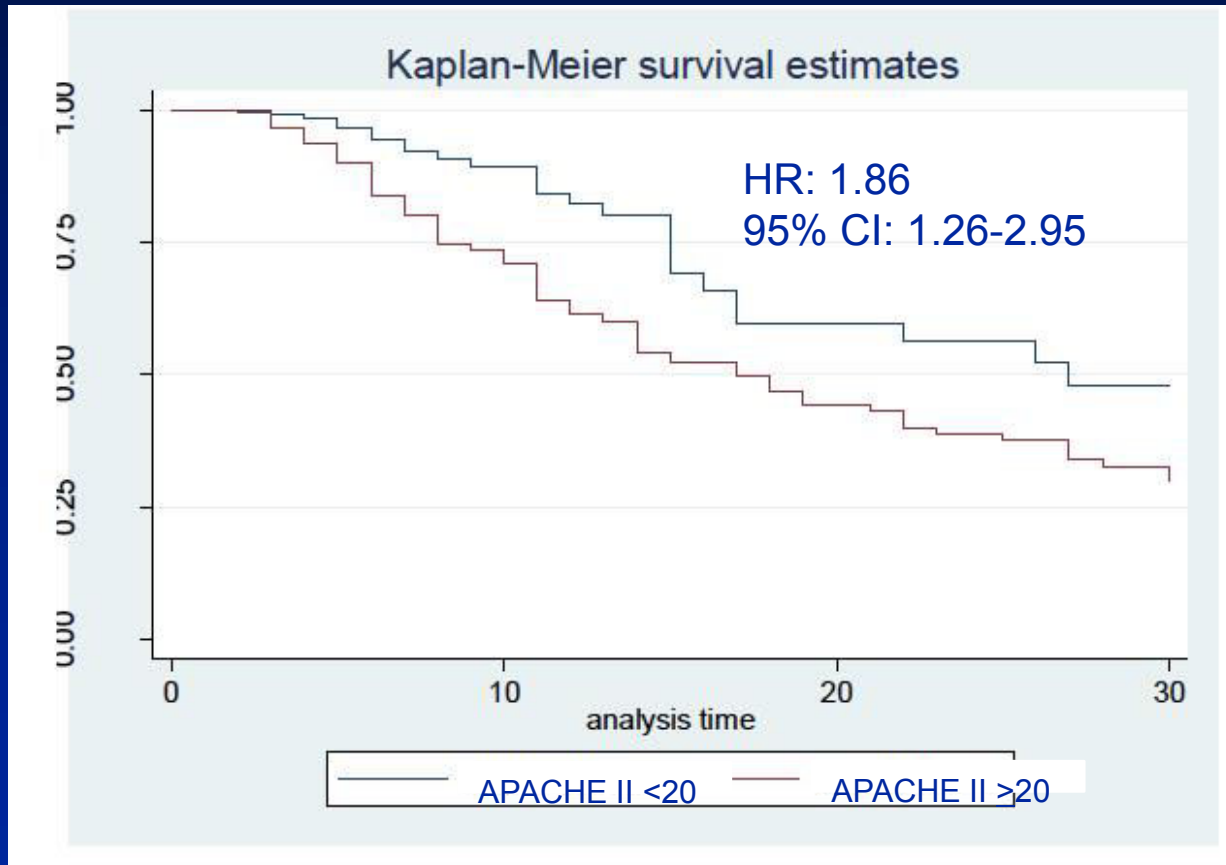
# Findings

- 6455 patient samples from 373 patients
- 1460 environmental and HCW's hand samples
  - Patient beds 5%
  - Table surfaces 2%
  - Pumps 0.4%
  - Telephones and keyboards 0.1%
  - Hands 1%
- Patients infected with *A. baumannii*
  - Colonization inanimate surfaces 38%
  - Patient colonization 60% ( $p < .001$ )

# Mortality vs Colonization vs Infection

Patient / Environment	Patients died in ICU n=144	Survived in ICU N=229	p
Infected w Acinetobacter	25 (17%)	28 (12%)	0.167
Colonized w Acinetobacter	69 (48%)	71 (31%)	0.001
Environmental colonization around patient beds	28 (20%)	19 (9%)	0.002

# Effect of APACHE II Scores on Survival at 30 Days



# Multivariate Analysis with Hospital Mortality in Infected Patients

## EPIC II Trial

Microorganisms		
<i>S. aureus</i>	0.82 (0.64-1.05)	0.12
MRSA	1.3 (0.94-1.8)	0.11
<i>S. epidermidis</i>	0.87 (0.69-1.1)	0.25
<i>S. pneumoniae</i>	0.84 (0.51-1.37)	0.47
<i>Enterococcus</i>	1.56 (1.07-2.27)	0.02
Gram +ve others	0.89 (0.65-1.23)	0.48
<i>E. coli</i>	0.89 (0.73-1.08)	0.23
<i>Enterobacter</i>	1.23 (0.93-1.63)	0.15
<i>Klebsiella</i> spp	1.01 (0.82-1.24)	0.94
<i>Pseudomonas</i> spp	1.38 (1.17-1.64)	<0.001
<i>Acinetobacter</i> spp	1.53 (1.2-1.95)	<0.001
Gram -ve, others	1.14 (0.95-1.37)	0.17
Anaerobes	0.92 (0.65-1.29)	0.62
Other bacteria	1.12 (0.62-2.03)	0.71
Candida	1.1 (0.91-1.32)	0.33
<i>Aspergillus</i>	1.71 (0.93-3.14)	0.08
Fungi: others	1.92 (0.97-3.79)	0.06
Parasites	1.34 (0.54-3.3)	0.53
Other organisms	0.89 (0.61-1.31)	0.56



# Factors Influencing Survival in MDR *Acinetobacter* Bacteremia

- **Observational study, February 2007-March 2008**
  - 100 *A. baumannii* complex bacteremia patients
  - Overall mortality 63% @14 days
- **Independent risk factors for mortality**
  - Diabetes mellitus (RR, 1.68; 95% CI, 1.22–1.76)
  - **Carbapenem resistance** (RR, 1.63; 95% CI, 1.19–1.89)
  - Septic shock (RR, 1.65; 95% CI, 1.23–1.85)

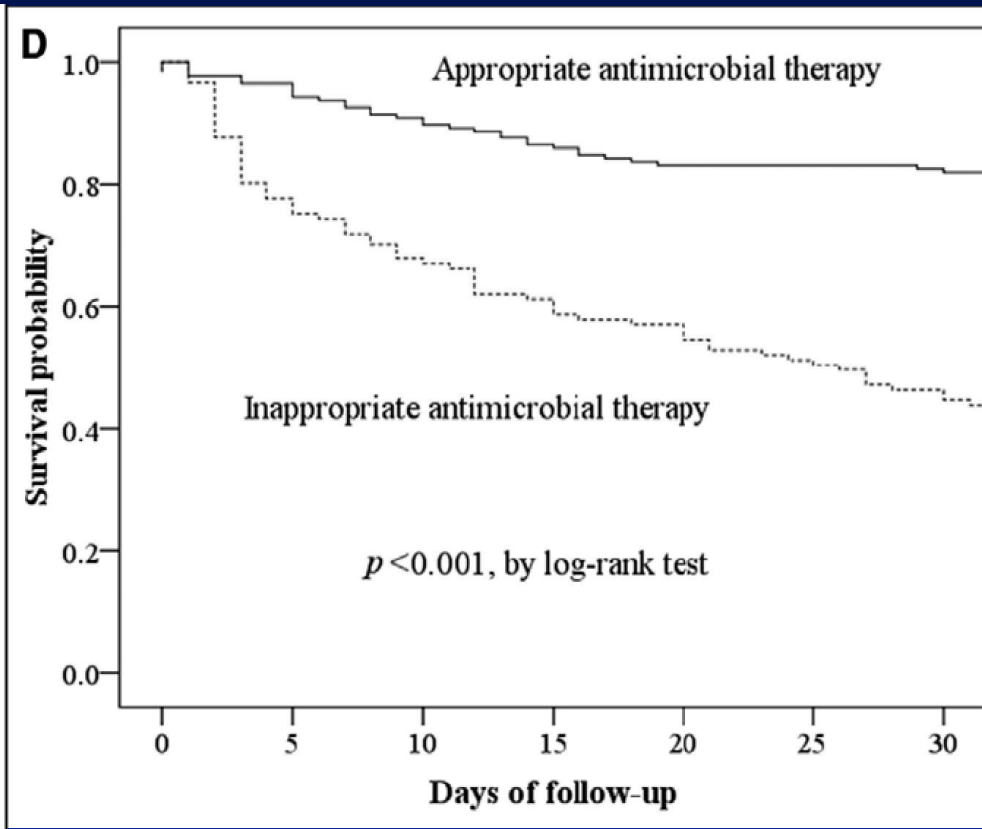
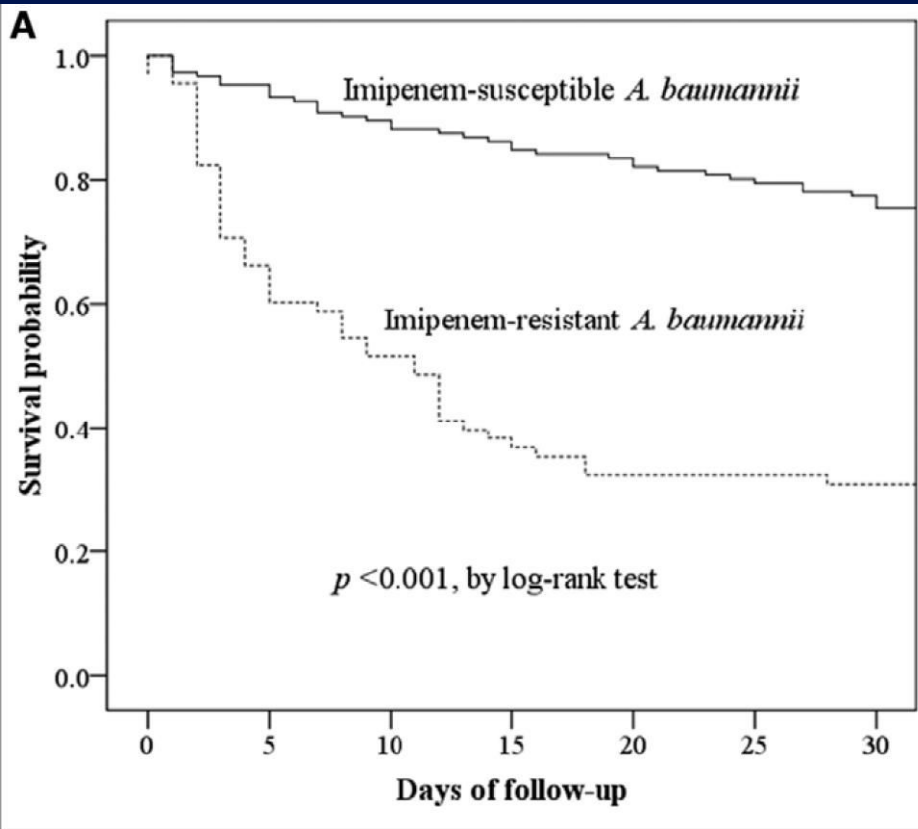
# Risk Factors for XDR *A. baumannii* Bacteremia

- 106 patients retrospective study, 2010- 2015
- Mortality with multivariate analysis
  - 7-day mortality (45.2%)
    - Shock (OR: 10.46, CI: [1.7-102.5], p .04)
    - Inappropriate definitive therapy (OR: 7.61, CI: [1.16-49.67], p 0.04)
    - History of immunosuppressive therapy (OR: 12.44 CI [1.91-81.13] p 0.008)
  - 30-day mortality (65.1%)
    - shock (OR: 8.01 CI [1.6-38.06] p .001)
    - malignancy (OR: 8.9 CI [2.2-36.61] p: <.001)

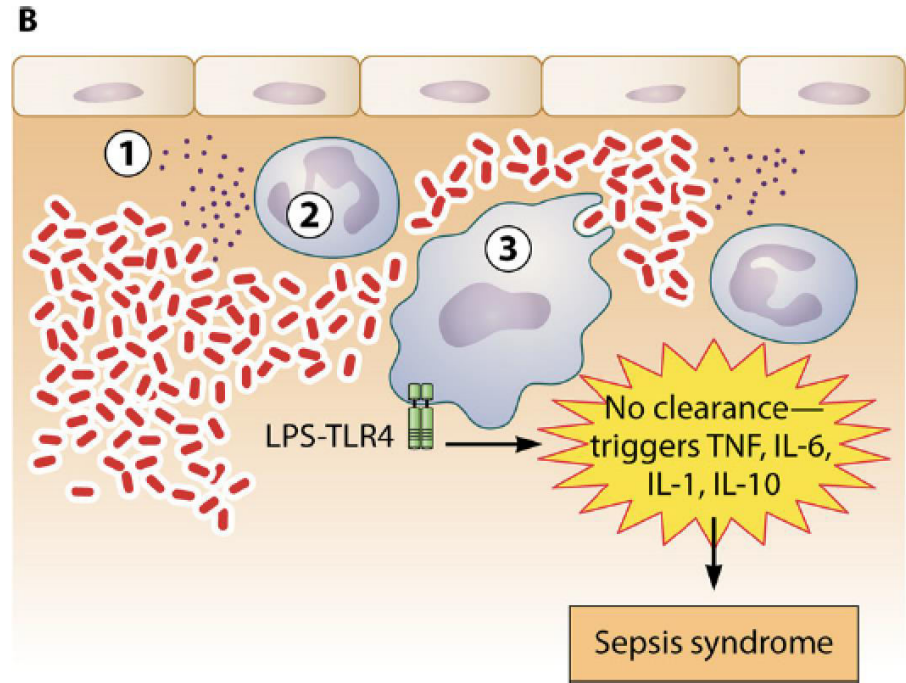
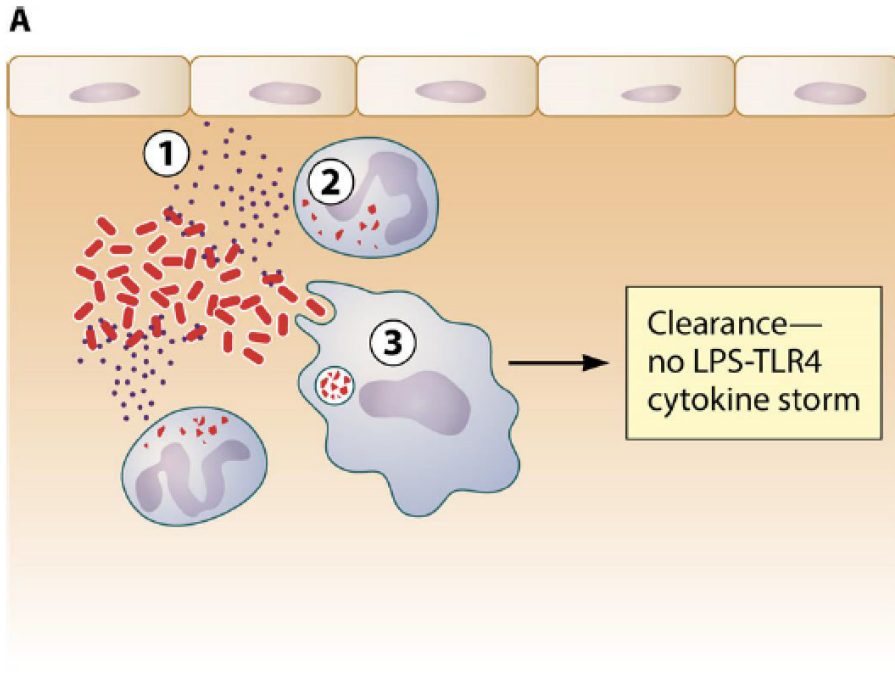
# Risk Factors and Outcome in *A. baumannii* Bacteremia

- 298 bacteremia cases, 2009-2010 in Taiwan
  - 73 (24.5%) with imipenem-R strains
  - 30 day mortality
    - 33.6% overall
    - 69.9% with imipenem-R strains
  - Mortality was not associated with any specific genotypes

# Survival in *Acinetobacter* Bacteremia



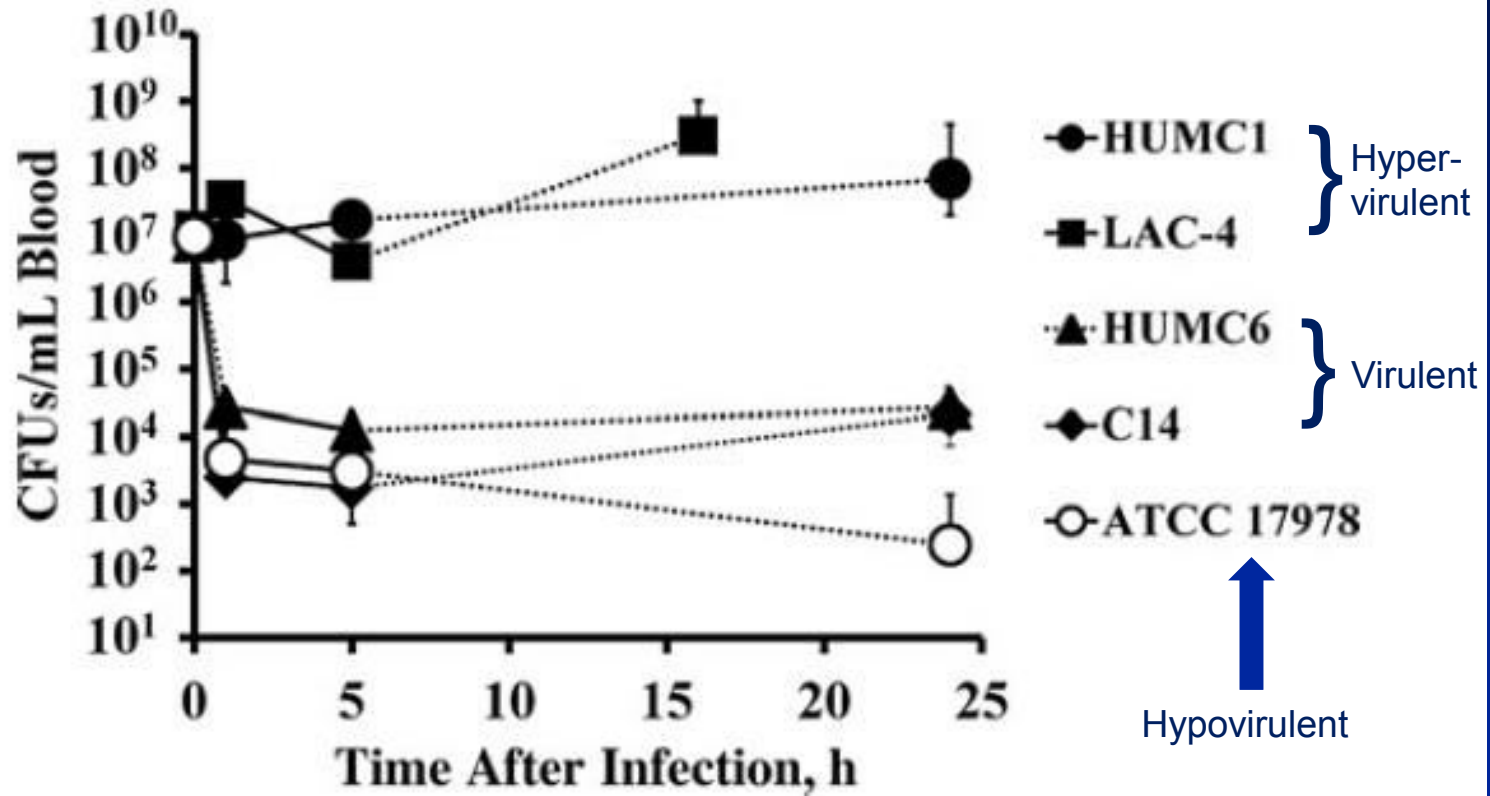
# Host Fate During Acinetobacter Infection



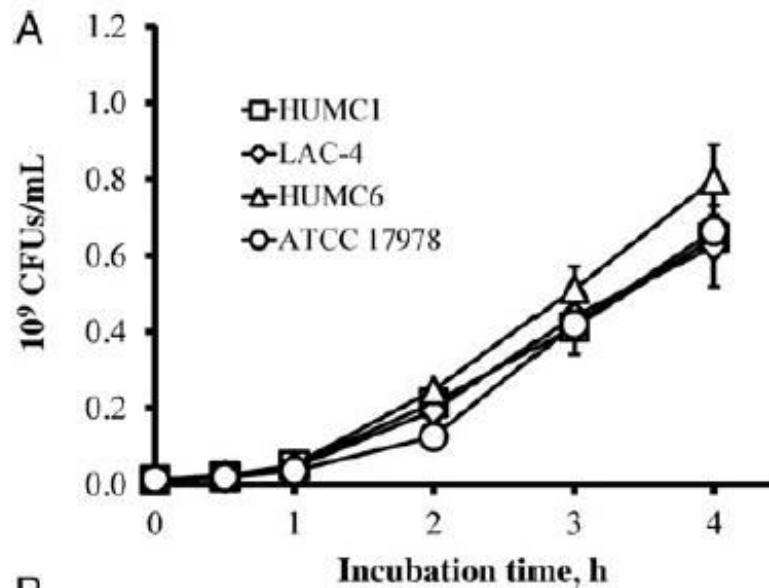
# Different Virulence Levels of *A. baumannii*

- **Hypervirulent**
  - 100% lethal BSI in mice within 3-d, with  $2 \times 10^7$  cfu, iv
- **Virulent**
  - 100% lethal BSI, with  $5 \times 10^7$  cfu
- **Hypovirulent**
  - Not lethal,  $>1 \times 10^8$  cfu

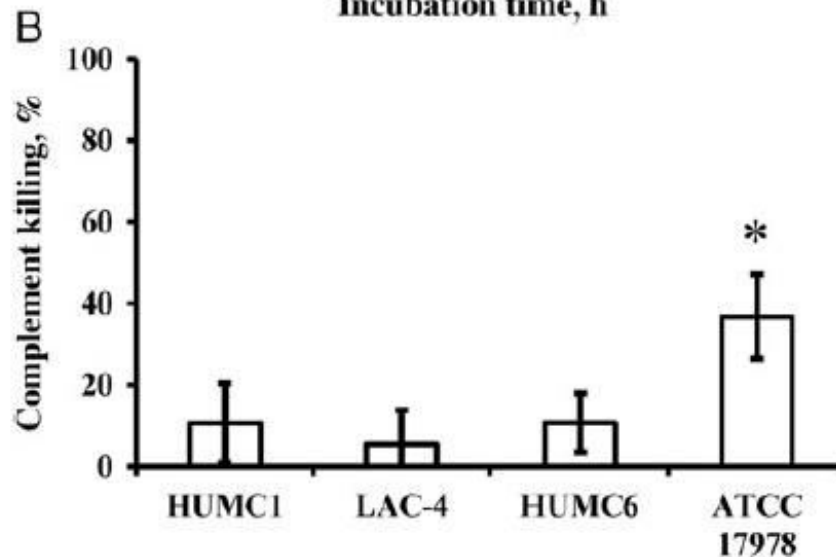
# Bacterial Counts of Different Strains of *A. baumannii* in the Blood of iv-Infected Mice



# Comparison of *A. baumannii* Strains



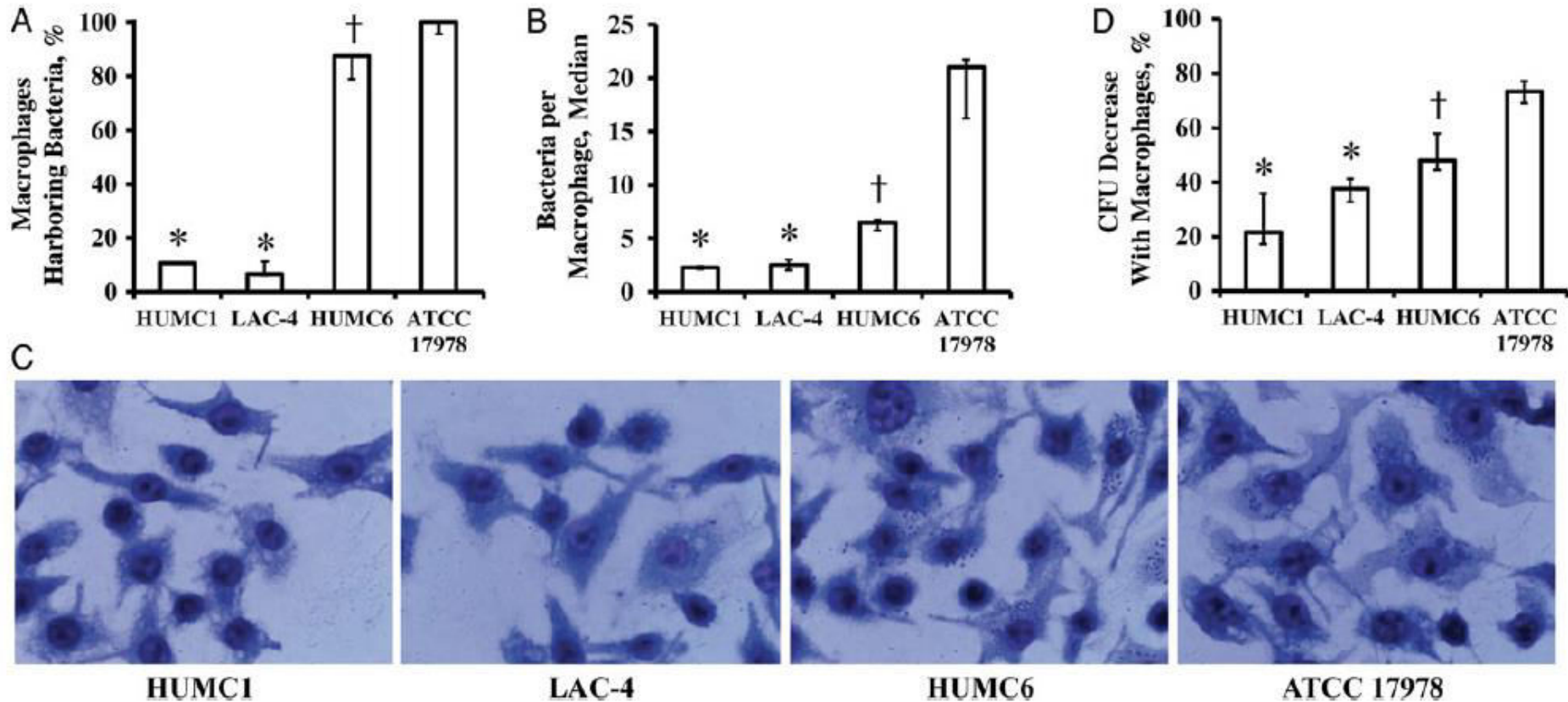
Growth rates



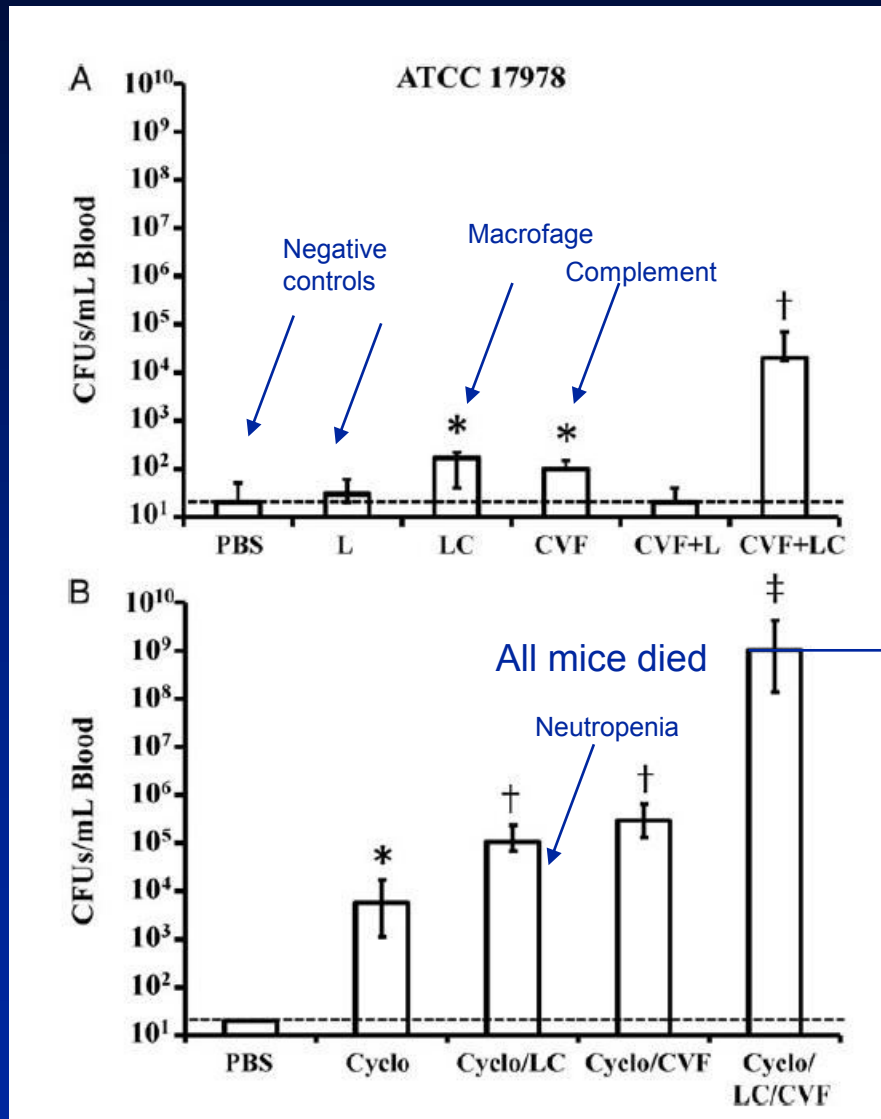
Complement susceptibilities



# Susceptibility of Different *A. baumannii* Isolates to Macrophage Uptake



# Impact of Innate Immune Disruption on Bacterial Densities



# Conclusions From the Current Study

- Hypovirulent *A. baumannii* strains can be converted to hypervirulent strains by triple disruption
  - Could lead much higher blood densities with hypo- and virulent strains
  - Less impact with hypervirulent strains
- Escape from host immunity is the primary virulence mechanism for persistence in the bloodstream

# Take Home Messages

- *A. baumannii* causes a huge clinical challenge
- Host- and bacteria related factors determine the outcome of infection
- Early effective treatment (if ever possible) may assist host rapidly clear bacteria
  - Avoids subsequent host damage by ensuing sepsis
- Ineffective early treatment causes persistence at high densities leading host damage

**Thank you...**