

Germ Wars - On a Planet Not So Far Away

The Battle Rages On

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The Aliens

- MRSA /GISA
- MRSE
- Resistant Pneumococcus
- VRE
- MDR GNR
- Quinolone Resistant GNR
- MDR TB
- Clostridium difficile

Pressures of Medical Care

- Rising costs
- Declining reimbursement
- Managed care
- Staff shortages
- Medicolegal issues
- Paper trail
- Quality of care
- Smarter germs . . . Newer germs

It takes the whole hospital to render quality medical care at the lowest cost.

Social Services
Infection Control Home Health
Pharmacy Administration Medical Staff
Nursing Micro Lab
Utilization Management

Infectious Disease Pearl of the Day

- The whole world is covered by a thin layer of feces, so . . . wash your hands!

When Did It Start?

- 1937 - Sulfonamide resistance in GC
- 1940's - PCN resistance in *S. aureus*
- 1980's - Extended spectrum beta-lactamases, VRE

Staph aureus - Leading the Way

- 1942 - Penicillin resistance
- 1947 - 75% resistance
- 1967 - 83% resistance
- 1982 - 90% resistance
- mid-1960's - methicillin resistance
- 1975 - 2.4% MRSA
- 1991 - 29% MRSA

Beta-Lactams – Mechanism of Resistance

- Alteration of PBP
- Alteration of porins
- Beta-lactamases (a) flood the periplasmic space, or (b) change the shape of the beta-lactamase

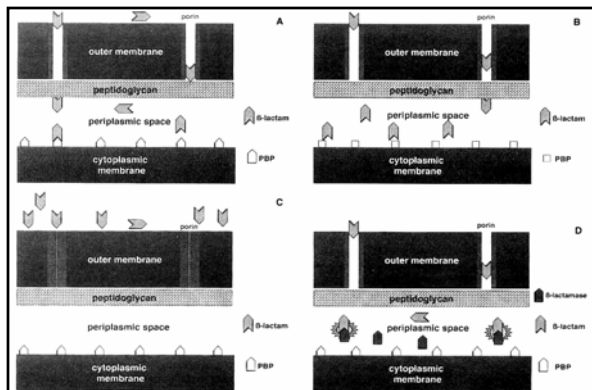


Figure 2. Resistance to β -lactam antibiotics. In the gram-negative cell, β -lactam antibiotics must enter through porins in the outer membrane, traverse the periplasmic space, and attach to their target penicillin-binding proteins (PBPs) located on the outer aspect of the cytoplasmic membrane (A). Resistance may arise through modification of the targets of the drugs, the PBPs (B), alterations in porin proteins that impede drug penetration into the cell (C), or the production of drug-activating enzymes, the β -lactamases (D).

Gram-Negatives

- PBP - Neisseria, Proteus
- Porins - specific (imipenem) or multiple drugs
- Beta-lactamases

Beta-lactamases (Bush Groups)

- Group 1 - intrinsically resistant to BLI's. Responsible for emergence of multiple BL-resistance. **Usually retain susceptibility to cefepime & imipenem**
- Group 2 - Intrinsically susceptible to BLI's. Carbapenem resistant. Mutants now resistant to ES cephalosporins

Beta-lactamases (Bush Groups)

- Group 3 - Carbapenem hydrolysis
- Group 4 - rare

**Clinical Relevance
Enterobacteriaceae**

- Inducible BL - emergence of resistance during therapy with ES cephalosporins
- Carbapenem resistance via carbapenemases, altered permeability, and altered PBP's

**Clinical Relevance
Enterobacteriaceae**

- Use of ceftazidime implicated in some outbreaks
- **Cefepime maintains activity against ESBL's**

Risk Factors for ESBL

Length of hospital stay
Length of ICU stay
Presence of central venous or arterial catheters
Emergency abdominal surgery
Presence of a gastrostomy or jejunostomy tube
Gut colonization
Low birth weight

Risk Factors for ESBL

Prior administration of any antibiotic
Prior residence in a long-term care facility (eg, nursing home)
Severity of illness
Presence of a urinary catheter
Ventilatory assistance
Undergoing hemodialysis

Clinical Relevance Enterobacteriaceae

- ESBL's do not attack cephamycins (e.g.-cefoxitin, cefotetan), porin loss causes development of resistance
- ESBL's encoded by plasmids that carry resistance to aminoglycosides, sulfonamides, chloro, tetracycline

Quinolone Resistance

- GyrA/GyrB
- parC/parE
- Permeability

Trends In Antibiotic Resistance in ICUs Nationwide 1994-2000

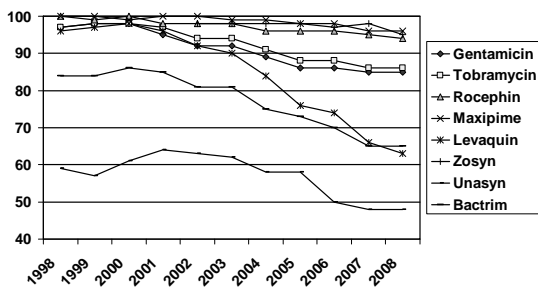
	All Isol	% chg	Ps aeru	Enterob
Cipro	81	-10	76	90
Tobra	83	-3	87	92
Zosyn	78	0	78	73
Max	78	+2	71	84
Roceph	59	-2	17	63

JAMA 289:885, Feb 2003

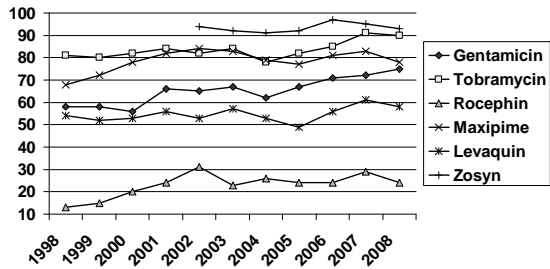
HBG Gram Negatives

	1998	2000	2002
Cefepime-E cloacae	100	96	94
Cefepime-Pseud aer	58	78	84
Cefepime-All	92	93	98
Rocephin-E cloacae	75	84	77
Rocephin-Pseud aer	19	20	31
Rocephin-All	78	84	90
Levaquin-Pseud aer	54	53	53
Levaquin-All	83	88	81

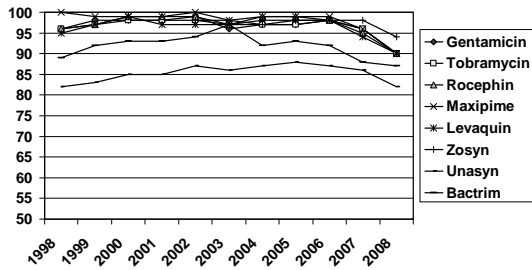
HBG E coli Susceptibilities



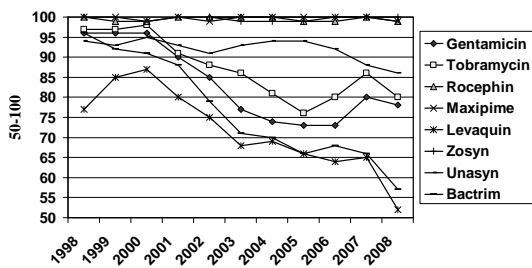
HBG Ps aeruginosa **Susceptibilities**



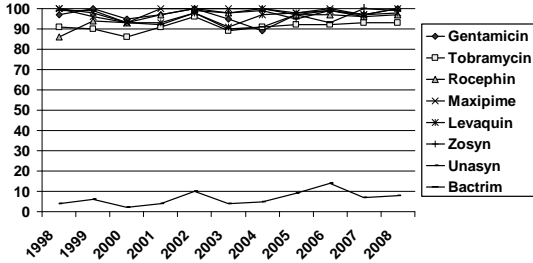
HBG K pneumoniae **Susceptibilities**



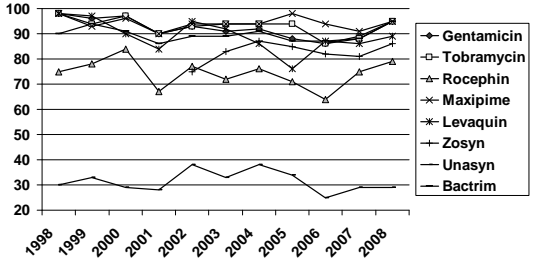
HBG P mirabilis **Susceptibilities**



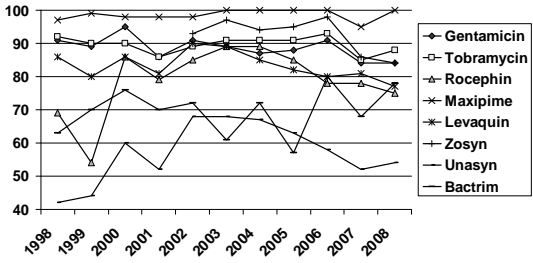
HBG S marcescens **Susceptibility**



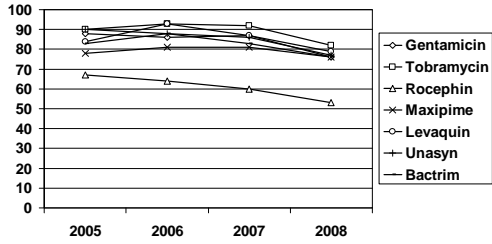
HBG E cloacae **Susceptibilities**



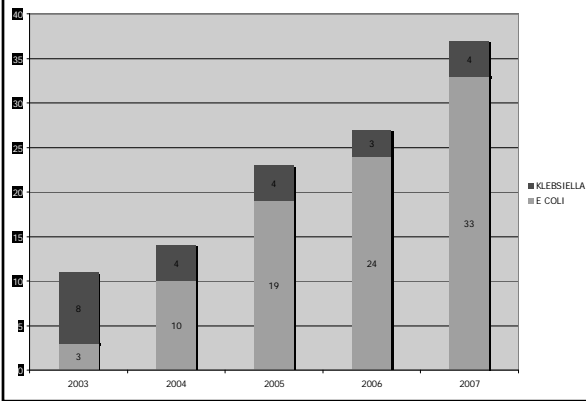
HBG C freundii **Susceptibilities**



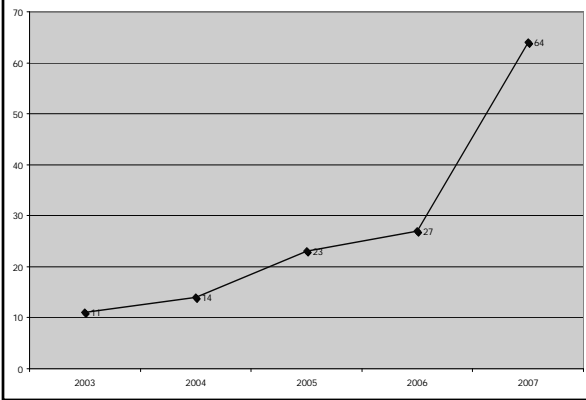
HBG Acinetobacter Susceptibilities

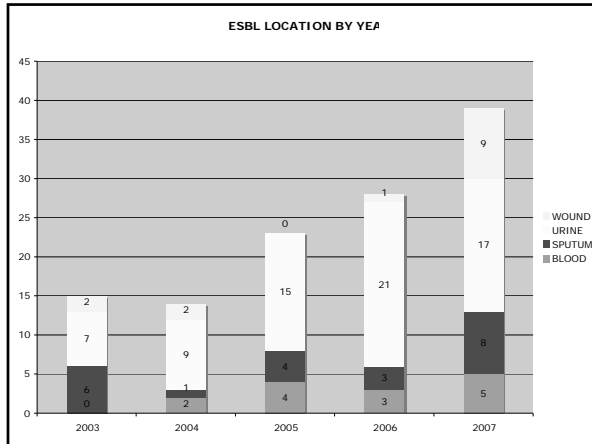


ESBL PRODUCERS IN HATTIESBURG



PREDICTED ESBL CASES THROUGH 2007





Resistance Patterns Dictate Antimicrobial Strategies

- Increasing resistance among gram-negative pathogens
 - Production of Bush group-1 β -lactamases (*Serratia*, *Pseudomonas*, indole-positive *Proteus*, *Citrobacter*, and *Enterobacter*)
 - Production of extended-spectrum β -lactamases (*E coli*, *K pneumoniae*)
- Suboptimal coverage against *P aeruginosa*

Jones RN et al. *Diagn Microbiol Infect Dis.* 1998;30:215-228.

Therapy for ESBL Infections

- Carbapenem
- High dose cefepime (inoculum effect)
- No data to support use of aminoglycoside
- ? Tigecycline

Shutting Down ESBL Outbreaks

- Barrier precautions
- Restricting oxyminocephalosporins

MDR Pseudomonas Therapy

Ticarcillin plus tobramycin plus rifampin
Polymyxin B plus rifampin
A fluoroquinolone plus either ceftazidime
or cefepime
Ceftazidime plus colistin
Clarithromycin plus tobramycin
Azithromycin plus one of the following:
tobramycin, doxycycline, trimethoprim,
or rifampin
Colistin plus rifampin



David Williamson Milne

On October 30, 2005 David Williamson Milne passed away at Kingston General Hospital after a battle with hospital-acquired infections. He was loved and is deeply missed by many.

David Milne was the kind of person that you got to know, and like, quickly. His friends were among society's small and society's great, and he treated each with equal respect and appreciation. His Scottish humour and laugh were infectious. Even in his last days he could make us laugh.

His family was the joy of his life and sustained him throughout. As the youngest of a large Manitoba farm family, he was his mother's joy and primary recipient of her loving largess. He wedded his first love and childhood sweetheart, Catherine, who followed him from posting to posting, with one a n d then two children, Catherine Jr. and Jacqueline.

As a long-service pilot in the Canadian Armed Forces David Milne's life was not without risk, but risk balanced in an equation with skill. His heart surgery was a risk, but it was balanced against the outstanding skill of Dr. Hamilton at Kingston General Hospital. The surgery was successful and Dave's recovery was proceeding well, thanks to the care of KGH staff. Unfortunately, a series of hospital-acquired infections set back his progress and ultimately caused his premature passing.

Every year hospital-acquired infections cause or contribute to the death of more people than breast cancer, heart disease, and car accidents combined. Most of these infections are initiated by otherwise caring healthcare workers who forget or neglect to clean their hands. And for each of those who, like our friend David, succumb to one of these unnecessary infections there are many more who ache for their loss. These are not numbers on month-end reports. These are our fathers, our mothers, our children and our dear friends who are dying prematurely because of unclean hands. The little bit of extra time that it takes for healthcare workers to wash or to use an alcohol sanitizer is pittance compared to the waste of so many productive, loved and loving lives.

In honour and memory of David Williamson Milne a donation will be made in his name to the Community and Hospital Infection Control Association of Canada. His family and extended group of friends openly urge those at Kingston General Hospital as well as healthcare workers everywhere to clean their hands before and after every patient contact. It is absolutely a matter of life and death.

Farewell to a dear husband, father and friend.

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What Lies Ahead?

- Novel classes of antibiotics
- Modification of known antibiotics
- Potentiators of known antibiotics
- New targets
- Inhibitors of virulence genes
- Antisense nucleotides

Preventing Drug Resistance in Hospitals

- Optimize antibiotic prophylaxis for surgery
- Optimize choice and duration of empiric Rx
- Improve prescribing by education
- Monitor and feedback info on antibiotic resistance rates
- Produce protocols for antibiotic usage

JAMA 275:234, 1996

Preventing Drug Resistance in Hospitals

- Develop systems to recognize and report resistance trends
- Develop systems to rapidly detect, report, and act on MDR bacteria in individual pts
- Improve compliance with basic infection control procedures and policies

JAMA 275:234, 1996

Preventing Drug Resistance in Hospitals

- Incorporate the detection, prevention, and control of antibiotic resistance into the institutions strategic goals
- Develop plans for identifying, transferring, discharging, and readmitting patients with resistant microorganisms

JAMA 275:234, 1996

Significant References

- **SHEA/IDSA** Position Paper for prevention of antibiotic resist-**ICHE 18:275-91 1997** or **www.sheaonline.org**
- **CDC/NFID** Strategy Paper on antibiotic resistance **JAMA 275:234-240, Jan 1996**
