Antibiotic Pressure and Resistance in Bacteria

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TDH CA-MRSA Conference
September, 2004
Antibiotic Pressure and Resistance in Bacteria

- What is it and why is it important?
- How extensive is it?
- How does it happen?
- What factors promote the spread of resistant bacteria?
- How does it pertain to the development of CA-MRSA infections?
- What can HCW do to curb this trend?
Antibiotic Pressure and Resistance in Bacteria

What is it?

• "Selection pressure of antibiotics has led to the emergence of antibiotic-resistant bacteria."

  – Antibiotics can effect bacteria unrelated to the targeted infectious agent; these may be “normal” flora, leading to the emergence of resistant mutants inhabiting the same environment.

Baquero et al., International Report 1996;23:819
Antibiotic Pressure and Resistance in Bacteria

Why is it important?

- Antibiotic resistance has developed in almost all classes of bacteria of pathogenic potential.
- Resistance in organisms of low virulence can emerge as important pathogens.
- The development of resistant bacteria has driven pharmaceutical research to develop more potent, broad-spectrum antibiotics.
- Use of these in turn, has fueled the appearance of bacteria with newer modes of resistance.
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Why is it important?

- Infections with resistant bacteria occur in health care settings AND the community.
- Examples of hospital setting: MDR Gram neg, MRSA, VRE
- Examples of community: MRSA, PRSP, Pcn R Quin R *N. gonorrhea*, antibiotic resistant *Salmonella* and *Shigella*
Emergence of Antibiotic-Resistant Bacteria

- *S. aureus*
- Gram-negative rods
- *N. gonorrhoeae*
- *H. influenzae*
- *M. catarrhalis*
- *S. pneumoniae*
- Enterococcus sp.

**Timeline:**
- 1950
- 1960
- 1970
- 1980
- 1990

- Penicillin
- Ampicillin
- 3rd gen Cephalosporins
- Quinolones

Cohen; Science 1992;257:1050
How extensive is the problem?

Percentage of Laboratory Isolates Resistant to Antibiotics, Texas

- Vancomycin-resistant Enterococcus Species
- Penicillin-resistant Streptococcus pneumoniae

![Bar chart showing percentage of laboratory isolates resistant to antibiotics in Texas from 1999 to 2001.](chart.png)
Scope of Problem: 
*S. pneumoniae*

- Most common cause of bactemia, bacterial pneumonia, meningitis, OM, sinusitis in childhood.
- Highest rates of invasive pneumococcal disease occur among young children, especially those aged <2 years
- US data: the seven most common serotypes isolated from the blood or CSF of children age <6 years account for 80% of disease
- Antimicrobial resistance is detected most frequently among these same serotypes.
- 1998 surveillance data from eight states: these serotypes accounted for 80% of penicillin-nonsusceptible isolates.
Percentage of Invasive Pneumococcal Isolates Nonsusceptible to Penicillin, Selected States, 1997

CDC, MMWR 1999; 48(30):656-661
Mechanisms of Bacterial Resistance: how DO they do it??
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*How does it occur?*

- All antibiotics do NOT kill bacteria in the same way.
- Various classes of antibiotics work on different aspects of bacterial replication.
Folic acid synthesis

DNA gyrase
Quinolones
DNA-directed RNA polymerase
Rifampin

Cell wall synthesis
ß-lactams & Glycopeptides (Vancomycin)

Trimethoprim

Folic acid synthesis

Sulfonamides

Protein synthesis inhibition
Macrolides & Lincomycins

Protein synthesis inhibition
Aminoglycosides

Protein synthesis inhibition
Tetracyclines

DNA
mRNA
Ribosomes

DHFA

THFA

PABA

DNA-directed RNA polymerase

DNA gyrase

Protein synthesis inhibition

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*How does it happen?*

- Bacteria can become resistant as a result of genetic mutations; these can be transferred between bacteria and groups of bacteria.
- Under selective pressure of antibiotic exposure, these strains then proliferate.
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*What happened to S. aureus?*

- Can become Resistant to the B-lactam drugs (PCNs, Cephalosporins) by making a B-lactamase.
- In response to development of a drug that is stable to this mechanism (methicillin/oxacillin), S. aureus alters its binding site (PBP): Methicillin Resistant S. aureus (*MRSA*)
- In response to use of other types of antibx to combat MRSA: few strains now with decr. sens to vancomycin, clindamycin.
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*What happened to S. aureus?*

- Reports of increasing use of third gen cephalosporins and quinolones related to emergence of MRSA.

- Some data suggest that quinolones enhance expression of methicillin resistance in SA *in vitro*

- *Outbreaks of MRSA have been reduced by curbing antibiotic use: esp cephalosporins*
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What factors promote their development and spread?

- Alteration of normal flora
- Practices contributing to misuse of antibiotics
- Settings that foster drug resistance
- Failure to follow infection control principles
Practices Contributing to Misuse of Antibiotics

- Inappropriate specimen selection and collection
- Inappropriate clinical tests
- Failure to use stains/smears
- Failure to use cultures and susceptibility tests
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Inappropriate Antibiotic Use

- Use of antibiotics with no clinical indication (e.g., for viral infections)
- Use of broad spectrum antibiotics when not indicated
- Inappropriate choice of empiric antibiotics
Inappropriate Drug Regimen

- Inappropriate dose - ineffective concentration of antibiotics at site of infection
- Inappropriate route - ineffective concentration of antibiotics at site of infection
- Inappropriate duration
Settings that Foster Drug Resistance

Community

- Day-care centers
- Long term care facilities
- Homeless shelters
- Jails
Settings that Foster Drug Resistance

- Intensive care units
- Oncology units
- Dialysis units
- Rehab units
- Transplant units
- Burn units
Physicians Can Impact

Patients

- Optimize patient evaluation
- Adopt judicious antibiotic prescribing practices
- Immunize patients

Other clinicians

- Optimize consultations with other clinicians
- Use infection control measures
- Educate others about judicious use of antibiotics
Controlling Pneumococcal Resistance—Iceland

Public campaign, physician education, and increased antibiotic cost

% nonsusceptible S. pneumoniae

Stephenson, JAMA 1996:275:175
Controlling Erythromycin Resistance in Group A Streptococci - Finland

Erythromycin consumption (DDD/1000)

Erythromycin resistance

Erythromycin consumption

Seppala, NEJM 1997;337:441
Antibiotic Pressure and Resistance in Bacteria:  
Conclusions

- Bacteria evolve resistance to antibiotics in response to environmental pressure exerted by the use of antibiotics.
- Many of these bacteria are significant pathogens.
- Our responsibility to our community is to use antibiotics prudently, for appropriate indications.