Antibiotic Resistance

Occurs when a microorganism fails to respond to a drug that it was previously susceptible to.

Not limited to hospitals, also seen in

- Nursing homes/extended care/rehab
- Community

Why do we care about antibiotic resistance?

Antibiotic Resistance: A Growing Concern

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Antibiotic resistance leads to

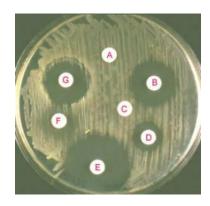
- Treatment failure
 - Poor outcomes
 - Increased mortality
- Increased need for combination therapy
- Increased cost of treatment

Antibiotic resistance is not new

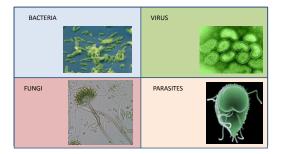
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4 types of microorganisms



Multidrug resistance

- Occurs when the microorganism is resistant to more than 1 class of antibiotics.
 - Betalactams (penicillin, cephalosporins)
 - Aminoglycides
 - Quinolones
 - Macrolides
 - Tetracyclines
 - Sulfonamides



Natural resistance to antibiotics

- Not every antibiotic works against every bacteria
 - Enterococcus do not have the binding site for cephalosporins
 - Vancomycin can't get thru the gram negative cell wall
- This natural resistance is not what we are concerned about, the concern is acquisition of new information

Acquired antibiotic resistance

A problem across all classes of microorganisms

- Staph aureus PCN, Methicillin, Vancomycin
- Strep pneumoniae PCN
- Tuberculosis MDR XDR
- Gonorrhea & Syphillis
- Salmonella, Campylobacter, E. coli
- Enterococcus faecium Vancomycin
- Pseudomonas many

Acquired resistance in other microorganims

Viruses

- HIV
- Influenza

Fungi

- Candida
- Parasites
- Malaria



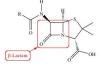
Bacterial Mechanisms of antibiotic resistance

- Inactivation of the antibiotic
- Alter the target site
- Alter the targeted metabolic pathway
- Pump the drug out
- Biofilm



Drug inactivation

- Penicillinase was 1st recognized in *Staph* aureus soon after the introduction of Penicillin.
- Beta-latamases an enzyme produced by the bacteria that breaks the beta-lactam ring of the antibiotic.



Alter the target site

- Antibiotic binds to the target and prevents that target from functioning normally
 - VRE the Vancomycin binding site is changed, the vanco can no longer work
 - MRSA mecA gene introduces a new PCN binding protien

Alter the targeted metabolic pathway

Turn the pump on!

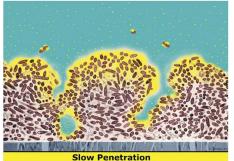
- Pumps are natural mechanisms in the cell
 - Tetracycline resistance is frequently a result of bacteria pumping the drug out.

Biofilms

- Biofilm is a complex matrix of organisms and extracellular polysaccharides (slime).
- Develop on hardware & invasive devices
- · Biofilms result in
 - Poor drug penetratior
 - Ability to evade host defenses



Antibiotic has difficulty reaching all the bacterial cells in a biofilm



Intrinsic (Naturally occurring)Resistance

- Does not require new genetic information
- May have been turned on in the presence of the antibiotic
 - pump mechanisms
 - Increase the production of the target

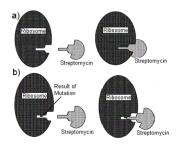
Acquired resistance

- Acquire new genetic material by
 - Mutation
 - Conjugation
 - plasmids
 - Transduction
 - Virus brings in
 - The DNA junk yard

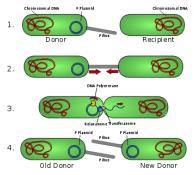


Mutation

• Spontaneous change in genetic material



Conjugation - Pass the Plasmid!!





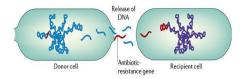
It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

Transduction

4

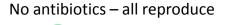
DNA Junk Yard

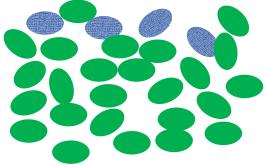
• Bacteria pick up genetic material from cells that have died.



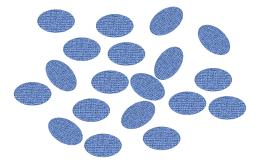
Selection of resistant organism







Antibiotic introduced



ESBL

Extended Spectrum Beta Lactamase

- Resistant to the 3rd & 4th generation cephalosporin
- Plasmid mediated
- >250 beta lactamases have been identified
- Seeing it in E. coli & Klebsiella and other members of the Enterobacteriaceae
- Risk factors
 - Prolonged hospital stay with ICU stay
 - Invasive medical devices
 - Previous antibiotic use

CRE

Carbapenem Resistant Enterobacteriaceae

- Rapidly emerging public health problem
- Plasmid mediated
- Several different mechanisms – KPC, VIM, NDM-1
- May require special testing to detect
- Resistant to many antibiotics



NDM-1 New Dehli metallo-beta-lactamase-1

- Resistant to most currently available
 antibiotics
- · Plasmid mediated
- Found in E. coli & Klebsiella pneumoniae
- · Felt to have originated in India
 - Overuse of antibiotics, poor hygiene & sanitation, over crowding
 - Medical tourism



They're not passengers arriving from a crash. They're part of our medical tourism travel package.

VISA VRSA Vancomycin intermediate/resistant SA

- Vancomycin has become the main treatment for Staph aureus infections
- VISA identified in 1996
- VRSA identified in 2002





IDSA's bad bug list ESKAPE ESCAPE

- Enterococcus faecium
- Staphylococcus aureus
- Klebsiella pneumoniae
- Acinetobacter baumannii
- Pseudomonas aeruginosa
- Enterobacter spp.
- Clostridium difficile
 Acinetobacter baumannii

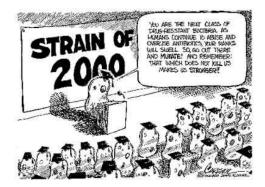
• Enterococcus faecium

• Staphylococcus aureus

- Pseudomonas aeruginosa
- Enterobacteriaceae

How did we get into this mess?

- Overuse of antibiotics
 - In humans
 - Patients who demand an antibiotic
 - Physicians who prescribe to keep patients happy or fear of negligence
 - Non-human uses
 animal feed
- Decrease in research & development of new antibiotics
 - Pharmaceutical companies won't invest
 - Regulatory agencies make it difficult to new antibiotics approved



Antibiotic Stewardship

Goals of antibiotic stewardship

- Optimize clinical outcomes
- Minimize unintended consequences
 - Toxicity
 - Emergence of resistance
 - Selection of pathogens (C.diff)
- Reduce cost

3 steps towards antibiotic stewardship

- 1. All antibiotic orders need dose, DURATION, and REASON
- 2. Whenever possible, GET A CULTURE
- 3. ANTIBIOTIC TIME OUT when culture is back
 - a. Is an infection unlikely?
 - b. Is this a resistant organism?
 - c. Can a narrower spectrum drug be used?



TENICILLIN 15 CALLED A WONDER DRUG " BECAUSE ANY TIME THE DOTOR WONDERS WHAT YOU'VE GOT, THAT'S WHAT YOU GET. "

Education for patients

- Give it a name Bronchitis caused by a virus - Explain why antibiotics are not needed
- Provide specific instructions for symptom relief
- Information about what to expect
- Information about when to call back





Infection Prevention

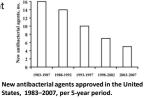
- HAND HYGIENE
- Standard Precautions

 appropriate use of Expanded Precautions
- Reduce the patients risk of developing an infection
 - Minimize use of invasive devices
 - Minimize use of antibiotics
 - Skin care

Antibiotic Development

- Encourage research and development
- Look at regulations that are getting in the way





Examine the non-human use of antibiotics



 Up to 70% of the antibiotics used in the USA are used in feed for animals (cows, pigs, chickens and other animals) to promote growth & prevent disease.

Antibiotics in the environment



Effective antibiotics are becoming a scarce resource

Use them wisely!