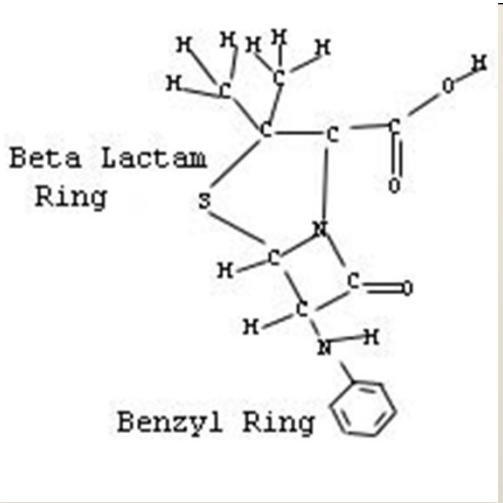
Antibiotic Use for a Sustainable Future

BtSM 2011

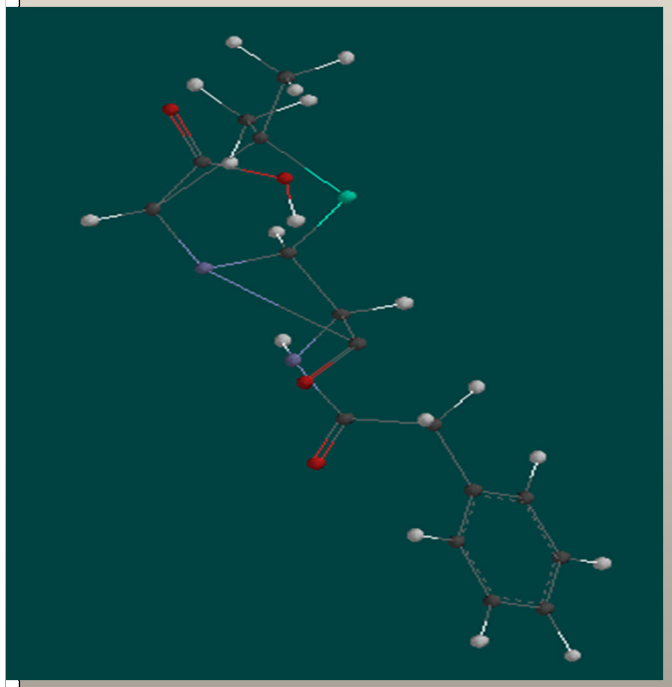
IMMEDIATE GLOBAL IMPORTANCE

Theme of WHO World Health Day 2011:

COMBATING ANTIMICROBIAL RESISTANCE



Antibiotic History



PENICILLIN

The image to the left is a structural model of penicillin G. Each ball is an atom, and each wire is a bond between the atoms. Grey atoms are hydrogen, red atoms are oxygen, black atoms are carbon, green atoms are sodium, and purple atoms are nitrogen. The ring shape in the bottom right corner is a benzyl ring, a set of six carbon atoms bonded into a ring shape. Other groups of atoms can appear on this end of the penicillin molecule. Different types of penicillin (ie, penicillin G, V, etc) have different structures there. The twisted ring in the upper region is called the beta lactam ring; it is the active area of the penicillin molecule. Every type of penicillin has the same beta lactam ring. Above is a chemical structure for the penicillin G molecule, in roughly the same form as the image to the right.

Discovered by Alexander Fleming in 1928.
Mold which killed Staph Aureus

Mechanisms of Resistance to ABX

- **Decreased penetration to the target site**
- **Alteration of the target site (penicillin binding protein, ribosome)**
- **Inactivation by bacterial enzymes (beta-lactamases)**
- **Efflux pumps**

How Fast Can Resistance Develop?

- **In 1946 6% of Staph Aureus were resistant to PCN.**
- **By 1960 60% of Staph Aureus were resistant to PCN.**

What Happened Next?

- **The Penicillin molecule was modified to counteract resistance.**
- **New penicillins such as methicillin and oxacillin were synthesized by the pharmaceutical companies.**

Emergence of Methicillin Resistant Staph Aureus

- First noted on the United Kingdom in 1961
- Epidemic in IVDA in the USA in 1981
- Now >50% of staph aureus in some hospitals are MRSA
- A CA (community acquired)-MRSA epidemic began in ~2000
- Resistance cassette carried on bacterial plasmids

Resistance in Gram Negative Rods

- **ESBL (extended spectrum beta-lactamases) – France 1984; USA 1988**
- **Carbapenemases – late 1990's are now worldwide**

TUBERCULOSIS

- **Mid 1990s – MDR-TB (multi-drug resistant tuberculosis)**
- **2006 – XDR-TB (extensively drug resistant TB) was noted at Tugela Ferry KwaZuluNatal in conjunction with the HIV epidemic. Now reported in 64 countries**
- **About 440,000 new cases of MDR-TB annually with >150,000 deaths**

MALARIA

- In most malaria-endemic countries resistance to chlorquine and fansidar (sulfadoxine-pyrimethamine) is now widespread
- Resistance to artemisinins is emerging in South-East Asia

Antiviral Resistant HIV

- **Likely?**
- **Use of tenofovir as a single agent in vaginal microbicides or as pre-exposure prophylaxis?**
- **Use of nevirapine to prevent mother-child transmission?**
- **National surveys are underway to detect and monitor resistance**

Why is this a serious problem?

- **AMR (antimicrobial resistance) can kill as infection fails to respond to usual treatment prolonging illness or resulting in death**
- **Control of infectious disease in the population is problematic as patients remain infectious for longer times, spreading microbes to others**
- **AMR increases the cost of health care as more expensive regimens for a longer duration and even surgery must be used**
- **AMR presages a return to the pre-antibiotic era making complex procedures such as transplants and cancer chemotherapy untenable**

What Practices Drive AMR

- **Inadequate national commitment, accountability, community engagement**
- **Inadequate or absent surveillance and monitoring systems**
- **Inappropriate and irrational use of antibiotics, including animal husbandry**
- **Poor infection preventative and control practices; poor laboratory quality assurance**
- **Inadequate systems to ensure quality and uninterrupted supplies of medicine**
- **Insufficient research and development of new products**

Antibiotic Stewardship Programs

- **Guidelines from the Infectious Disease Society of America**
- **Address the control of AMR through rational use of antibiotics**
- **Evidence based**
- **Professional advice/control**
- **Since there are few data on outpatient/long-term care facilities, only provides guidelines for hospital-based use**

Antimicrobial Stewardship Strategies

- **Prospective audit with intervention and feedback**
- **One-on-one education of housestaff/attending in a patient-specific basis by an infectious disease specialist and/or clinical pharmacist reviewing microbiologic data, local resistance patterns and clinical literature**
- **Advice given on appropriateness of the regimen, route of administration, dosing, duration toxicity monitoring**
- **Audit triggered by computer surveillance of antibiotic ordering**
- **Daily review preferred; 120-bed community hospital reviewed 3x/week**
- **Several studies showed cost saving, for example one controlled study showed a saving of $400/patient with no adverse impact.**
- **A-1 evidence in favor of this option**

Antimicrobial Stewardship Strategies

- **Formulary restriction and preauthorization**
- **Can lead to immediate cost reduction**
- **May be beneficial in a multi-faceted response to a specific nosocomial outbreak**
- **Might just shift use to an alternative agent to which bacteria then develop resistance. For instance: restricting ceftazidime has led to use of imipenem and emergence of imipenem resistant pseudomonas**
- **Thus require careful monitoring**

Antimicrobial Stewardship Strategies

- **Education**
- **Education is elemental to the acceptance of stewardship strategies**
- **However education alone without active intervention has proven only marginally effective and has not demonstrated sustained impact.**

Antimicrobial Stewardship Strategies

- **Guidelines and clinical pathways**
- **Multidisciplinary development of practice guidelines incorporating local microbiology and resistance patterns can improve antimicrobial utilization**
- **Guideline implementations can be facilitated through provider education and feedback on patient outcomes**

Antimicrobial Stewardship Strategies

- **Other effective strategies:**
- **Streamlining and de-escalating therapy when culture results available**
- **Conversion from parenteral to oral therapy when the patient's condition allowed, freeing the patient from the hospital environment**
- **Dose optimization based on patient's characteristics (weight, site of infection, renal and hepatic function), microbial MIC, pharmacokinetics of agent and method of killing**

INEFFECTIVE STRATEGIES

- **Antibiotic cycling – concept of changing antibiotics available in hospital from month to month**
- **Combination therapy only effective for increasing the breadth of coverage and likelihood of adequate initial therapy, not for decreasing the development of resistance.**

RECOMMENDATONS FROM IDSA

(Infectious diseases society of America)

- **Multidisciplinary team to include an infectious diseases physician and a clinical pharmacist with infectious diseases training who should be compensated for their time with inclusion of a clinical microbiologist, IT specialist, an infection control professional and a hospital epidemiologist is optimal.**
- **Collaboration of this team with hospital infection control and pharmacy and therapeutic committee is essential.**
- **Support of the hospital administration, medical staff leadership, local providers essential. Desirable to function under quality assurance and patient safety dept.**
- **Administration must offer support for the infrastructure to measure and track antimicrobial use in real-time.**
- **Administration must grant adequate authority and compensation to the team and delineate expected outcomes for the program.**