INTRODUCTION

The worldwide epidemic of antibiotic resistance carries the danger of ending the golden age of antibiotic therapy. Resistance has impacts on all areas of medicine, and is making successful empirical therapy much more difficult to achieve. Antibiotic choices are often severely restricted, and the pipeline of new antibiotics is almost dry. Resistance cannot be prevented, but its development and spread can be slowed ***(Boucher et al., 2009)***.

Thus we have no alternative but to use antibiotics more wisely. Antibiotic stewardship can offer more than an effect on resistance by interventions and programs designed to improve antibiotic use. It can also reduce pharmacy costs, toxicity and the acquisition of potentially pathogenic bacteria by preserving the normal protective bacterial flora ***(Gould, 2008)***.

The emergence of drug resistance among nosocomial pathogens is an increasing problem. The increase in antibiotic resistance among gram negative bacteria is a notable example of how bacteria can procure, maintain and express new genetic information that can confer resistance to one or several antibiotics ***(Poole, 2003).***

Infections caused by gram-negative bacteria have features that are of particular concern. These organisms are highly efficient at up-regulating or acquiring genes that code for mechanisms of antibiotic drug resistance, especially in the presence of antibiotic selection pressure. Furthermore, they have available to them a plethora of resistance mechanisms, often using multiple mechanisms against the same antibiotic or using a single mechanism to affect multiple antibiotics ***(Peleg and Hooper, 2010).***

The extended spectrum beta lactamases (ESBL) are the B-lactamases capable of conferring bacterial resistance to the penicillins, 1st, 2nd and 3rd generation cephalosporins and aztreonam (but not the cephamycins or carbapenems) by hydrolysis of these antibiotics, and which are inhibited by B-lactamase inhibitors such as clavulanic acid ***(Bush et al., 1995).***

This property differentiates the ESBLS from the AmpC type B-lactamases which have third generation cephalosporins as their substrates but which are not inhibited by clavulanic acid ***(Cosgrove et al., 2002)***.

Organisms with plasmid mediated AmpC enzymes are generally resistant to broad spectrum penicillins, extended- spectrum cephalosporins, monobactam, and cephamycins but are susceptible to cefepime, cefpirome, and carbapenems ***(Philippon and Jacoby, 2002).***

Based on molecular studies two types of carbapenem hydrolyzing enzymes have been described. Serine enzymes possessing a serine moiety at their active site (class A, Class D) and metallo B-lactamases (MBLS, Class B), requiring divalent cations, usually zinc as metal cofactors for enzyme activity ***(Bush, 2001).***

The proportions of both hospital acquired and community acquired infections caused by methicillin- resistance *staphylococcus aureus* (MRSA) have steadily been increasing worldwide. Infections caused by MRSA result in longer hospital stays, rising health care costs and have a high attributable mortality rate ***(Deresinski, 2005).***

Vancomycin resistant *Enterococci* (VRE) is a mutant strain of *Enterococcus* that originally developed in individuals who were exposed

to the antibiotic. It was 1st identified in Europe in 1986 and in the U.S in 1988 ***(Showsh et al., 2001).***

The development of vancomycin-resistant *enterococci* led the way to the emergence of vancomycin-resistant *S. aureus* (VRSA) with (MIC) ≥32 μg/mL) ***(NCCLS, 2003).***