STRATEGIES TO OVERCOME ANTIMICROBIAL RESISTANCE IN VETERINARY PRACTICE

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Antimicrobial resistance occurs when microorganisms such as bacteria, viruses, fungi and parasites change in ways that render the medications used to cure the infections they cause ineffective. This is a growing global concern because a resistant infection can spread to others, can become lethal and imposes huge costs to individuals and society. A microorganism that develops resistance to all available antimicrobial is often referred to as "superbug". Antimicrobial resistance is not a new problem but one that is becoming more dangerous; urgent and consolidated efforts are needed to avoid regressing to the pre-antibiotic era.

Consequences of Antimicrobial Resistance

1. In both humans and animals, antimicrobial resistance development will result in increased death rates and diseases because effective therapy for specific infections is delayed or unavailable. All humans and animals have populations of normal bacteria in and on their bodies. A more subtle effect of resistance on the incidence of disease occurs when a person or animal receives an antimicrobial drug to which a potentially infective or colonizing bacteria is already resistant.
2. Development of resistant bacterial varieties will cause the need for newer drugs and the development of which invariably results in higher costs both for drug developing companies and for the patients. Also it is a complex and time consuming affair in addition to the burden of controlling the spread of resistant isolates (Armyes and Gemmell, 1992)

Emergence of Antimicrobial Resistance

Bacteria are highly versatile in their genetic makeup and so can easily develop resistance. All bacteria have an inherent flexibility that capacitates them to evolve genes that render them resistant to antimicrobials sooner or later. Bacteria can incorporate DNA from different species and even different genera into their own genetic make-up. Also they multiply very rapidly and if the conditions are ideal they can double in 20 minutes. If even one bacteria in a billion is able to survive exposure to an antimicrobial by becoming resistant, then its descendants will quickly reproduce. The use of antimicrobials in human and animals for the last five decades has encouraged the multiplication and spread of resistant strains (Krause, R.M., 1992)

Mechanisms of Antimicrobial resistance

Two major forms of Antimicrobial resistance are mutational and transmissible. Mutational resistance occurs from chromosomal mutations in the bacterial DNA that are then transmitted to progeny during replication. This form of resistance develops slowly step by step and requires long time exposure to an antimicrobial to become clinically significant.

E.g.: Clinical resistance to fluoroquinolone antimicrobials occurs from chromosomal mutations.

Transmissible resistance is more rapid to develop and requires genetic exchange between bacteria. Most of the antimicrobial resistance can be attributed to this form of resistance. Bacteria can transmit the transmissible antimicrobial resistance genes by four different mechanisms: transformation, transduction, conjugation and transposition (Murray, B., 1991)

Current Scenario in Antimicrobial Resistance

Many global trends have helped to accelerate the spread and speed of infection, including factors such as urbanisation (eg: overcrowding, poor sanitation etc),

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Pollution, Environmental degradation , Weather patterns (affecting the incidence and distribution of infection) , 'inappropriate' use of antimicrobials also contributes to the problem - this occurs when they are taken for too short a time, at too low a dose, at inadequate potency, or for the wrong disease, poor infection prevention and control practices .

Resistance to earlier generation antimalarial medicines such as chloroquine and sulfadoxine-pyrimethamine is widespread in most malaria-endemic countries. Falciparum malaria parasites resistant to artemisinins are emerging in South-East Asia; infections show delayed clearance after the start of treatment (indicating resistance). During the past 3 decades, MRSA (methicillin-resistant Staphylococcus aureus) has created significant epidemiological, infection-control, and therapeutic management challenges.

Another paper published recently by Kumarasamy *et al*. (2010) highlights the serious threat posed by the NDM-1 (New Delhi metallo-â-lactamase-1) superbug, a microbial threat for which there is limited surveillance and no effective treatment. NDM-1 is a recent entrant in the family of superbugs and produces an enzyme called Metallo-beta-Lactamase-1 (MDM-1). This enzyme helps these bacteria to destroy the most potent antibiotic carbapenem, known to kill most of the known bacteria. *E.coli* and *Klebsiella pneumoniae* are the two bacteria which hosts this enzyme. MDM-1 enzymes are produced by strands of DNA which bacteria are known to transfer between one another. So this superbug has the potential to get copied and transferred between bacteria, allowing it to spread rapidly. The superbug was named as New Delhi Metallo-beta-Lactamase-1(NDM-1) after the national capital (New Delhi), where a Swedish patient was reportedly infected after undergoing a surgery in 2008. Most of other patients had carried this infection from India, Pakistan and Bangladesh.

Western European countries have managed to decrease the rate of antimicrobial resistance in some pathogens through a multipronged approach in comprehensive well regulated health systems. Integrated monitoring of antibiotic consumption and resistance, prescriber and consumer education that is coordinated and paid for by the government and regulation of use in communities and hospitals have shown that it is possible to contain antimicrobial resistance. Pharmacists readily dispense antibiotics without prescription in the developing world as their income depends on sales rather than on a professional fee or salary. Pharmaceutical companies may promote sales of antibiotics independent of patient need. Finally, most antibiotics, by virtue of their safety and short courses, lend themselves to abuse; patients often take antibiotics of their own accord. Improved drug access without significant improvements in appropriate use will have dire consequences, with continued emergence of "superbugs" and untreatable infections. Sub-therapeutic doses of antibiotics are used in animal-rearing for promoting growth or preventing diseases. This can result in resistant microorganisms, which can spread to humans.

WHO Scientific Working Group guidelines for the use of antibiotics in Veterinary field:

a) Antibiotics for veterinary use should be available only on prescription by a licensed person; training courses for these persons should be organized by the national authorities

b) Countries should be encouraged to prohibit the therapeutic use in animals of certain newer antibiotics that are required for the treatment of serious infections in man (eg.,gentamicin and related aminglycosides, spectinomycin, rifampicin); Chloramphenicol should be reserved for use in man, as this antibiotic is still widely used for the oral treatment of salmonellosis in animals, its use should be restricted to the treatment of infected animals under the care of a veterinary surgeon and the drug should be available for such use only as a parenteral preaparation

c) Since large numbers of antibiotic preparations are available for mastitis, the use of fixed-ratio combinations of antibiotics should be discouraged

d) The routine use of antibiotics prophylactically, in the absence of proven infection, should be avoided

Combating antibiotic resistance

The following are recommendations to combat the development of antibiotic resistance in bacteria and other microorganisms

- To combat the occurrence of resistant bacteria biotechnology and pharmaceutical companies must constantly research develop and test new antimicrobialsi no rdert om aintaina p oolo f effective drugs on the market
- Stopt heu seo fa ntibioticsa sg rowth promoting substances in farm animals Of major concern is the use of antibiotics as feed additives given to farm animals to promote animal growth and to prevent infections rather than cure infections The use of such antibiotics contributes to the emergence of antibiotic resistant bacteria that threaten human health and decreases the effectivenesso ft hes amean tibioticsu sedt o combat human infections
- Use the right antibiotic in an infectious situation as determined by antibiotic sensitivity testing when possible
- Stop unnecessary antibiotic prescriptions Unnecessary antibiotic prescriptions have been identified as causes for an enhanced rate of resistance development Unnecessary prescriptions of antibiotics are made when antibiotics are prescribed for viral infections antibiotics have no effect on viruses This gives the opportunity for indigenous bacteria normal flora to acquire resistance that can be passed on to pathogens
- Compliancew itht hep rescriptionI t is important to c omplete t he f ull c ourse o f t he d rug Unfinished antibiotic prescriptions may leave some bacteria alive or may expose them to sub inhibitory concentrations of antibiotics for a prolonged period of time Mycobacterium tuberculosisi sa s lowg rowingb acteriaw hich infects the lung and causes tuberculosis Large scale public health education efforts are underway to stress the importance of finishing prescriptions
- Optimization of infection control practices and immunization programmes

On World Health Day (7th April 2011), WHO will issue an international call for action to halt the spread of antimicrobial resistance and it will focus on recommending a six-point policy package for governments in future. However, the war against antimicrobial resistance will have to be fought as long as we must depend on these drugs as our primary means of treating infections.

REFERENCES

Armyes,S.G.B., Gemmell,C.G. 1992 Antibiotic resistance in bacteria. *J. Med. microbiol*, 36:4-29

Clifford McDonald.L., 2006 Trends in Antimicrobial Resistance in Health Care Associated Pathogens and Effect on Treatment.,*Clinical Infectious Diseases* Vol.42 **2**: S65-S71

Control of antibiotic-resistant bacteria: Memorandum from a WHO Meeting, 1983, Bulletin of the World Health Organization, 61**3** : 423-433

Krause, R.M., 1992 The origin of plagues: old and new. *Science*, 257: 1073-1078

Kumarasamy KK, Toleman MA, Walsh TR, *et al*. Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study. *Lancet Infect Dis* 2010; 10:597-602.

Murray,B.E. 1991 New aspects of antimicrobial resistance and the resulting therapeutic dilemnas. *The j. Infect. dis*, 163: 1185-1194

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