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Antimicrobial (Drug) Resistance

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Introduction

Antimicrobial resistance (AMR) is the ability of living microbes, including bacteria, virus, fungi and parasites to grow in the presence of a chemical that would normally kill or limit its growth. Resistance to antimicrobial drugs is now widespread in both developing and developed nations and because of AMR many infectious diseases are difficult to treat. This is an ever increasing threat to global public health and, requires action across all government sectors and society. AMR is considered a serious threat to society because infections caused by resistant microorganisms often fail to respond to standard treatment and this ultimately results in higher healthcare expenditure, prolonged illness, and more importantly greater risk of death [1]. According to the Centers for Disease Control and Prevention (CDC), antibiotic resistance costs the U.S. healthcare system in excess of $20 billion annually, $35 billion in other societal costs and more than 8 million additional days spent in the hospital. This mini review mainly focuses on the present issues regarding antimicrobial drug resistance and pin-points the available drugs for various infections caused by bacteria, parasite, virus and fungi.

AMR in Bacteria

Multi-drug resistant Tuberculosis (MR-TB) strains have been identified globally with varying degrees of frequency. The two commonly used antibiotics (Isoniazid and Rifampin) are often no longer effective in the treatment of TB. Extensively drug-resistant Tuberculosis (XDR-TB) is less common and it is resistant to the second-line drugs such as Fluoroquinolone [2]. However, the two recently evaluated drugs, Clofazimine and Amoxicilline with Clavulanate have shown clinical efficacy in the treatment of MDR and XDR-TB [2,3].

Methicillin-resistant *Staphylococcus aureus* (MRSA) has developed into a serious health issue during the past few decades. Currently, healthcare providers are prescribing beta-lactam antibiotics as a first line of defense, Vacomycin administered intravenously for more severe forms. Challenges in treatment include the emergence of new resistant strains and increased nephrotoxicity. Prior to the use of beta-lactam antibiotics, Linezolid and Daptomycin were effectively used for the first line of treatment [4,5]. Ceftaroline is the newest FDA approved cephalosporin antibiotic for the treatment of community acquired pneumonia and acute bacterial skin infections [6].

Unlike *Staphylococcus* or *Escherichia coli* (*E. coli*), *Enterococci* infections are most commonly acquired among the hospitalized patients. *Enterococci* are of special interest because they also pose the issue of antibiotic resistance, such as Vancomycin-resistant *Enterocci* (VRE). Linezoid is the most frequently used antibiotic in VRE treatment [7,8]. Tigecycline is an effective alternative to Linezoid [9].

Multidrug-resistant *Neisseria gonorrhea* appears to be the second most common sexually transmitted infection of bacterial origin in the world today [10]. Currently, in the United States, most cases are treated with the combination of Cephalosporin and Azithromycin or Doxycycline [11]. Multidrug-resistant infections (Cephalosporin-resistant infections) can be treated with the combination of existing antibiotic therapies such as Gentamicin and Azithromycin or Gemifloxacin and Azithromycin [12].

AMR in Malaria

Three of the five species known to cause malaria have been documented as being capable of developing resistance to anti-malarial drugs (*P. falciparum*, *P. vivax* and *P. Malariae).* The World Health Organization (WHO) recommended anti-malarial drugs for the treatment of uncomplicated malaria, are the Artemisinin-based combination therapies (ACTs). However, *P. falciparum* resistance to first-line malarial drugs, namely Arteminsinin, is now emerging as an urgent public health concern [13]. Currently, four treatment options are available for malaria. The first treatment option is *Chloroquine (Aralen),* and it is routinely used for uncomplicated malaria acquired in areas without Chloroquine resistance. For *P. falciparum* infections resulting from Chloroquine-resistance strains, Atovaquone-Proguanil (Malarone) or Artemether-Lumefantrine (Coartem) can be used in non-pregnant adult and pediatric patients. Quinine sulfate plus Doxycycline (Vibramycin), Tetracycline, or Clindamycin are other viable options. A fourth option is Mefloquine (Lariam). These treatments come with the issue of possible, neuropsychiatric reactions. No Chloroquine resistance strains of *P. vivax* and *P. Malariae*, have been reported therefore, Chloroquine remains an effective treatment for these species [14].

Anti-Viral Drug Resistance

Viruses constantly evolve resulting in new strains during each active season. This means that vaccines are not often useful after single season of treatment. The Influenza virus is prime example of this phenomenon. In the United States, three FDA approved anti-viral drugs are available including, Oseltamivir (Tamiflu) [15], Zanamivir (Relenza) [16] and Peramivir (Rapivab) [17]. However, some Oseltamivir resistant H1N1 viruses were detected during the 2013-2015 season. The most recent influenza-strain identified is still susceptible to neuraminidase inhibitors including the anti-viral drug (Oseltamivir) [18].

Anti-Fungal Drug Resistance

Unlike, AMR in bacterial infections, anti-fungal drug resistance is less common. However, invasive fungal infections, such as those caused by *Candida* do pose a serious health issue. Candidemia, a *Candia albicans* infection of the blood stream, can result in an additional 3 to 13 days of hospitalization with health-care cost $6000 to $29000

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[19]. *Candia* has become increasingly resistant to first and second-line anti-fungal treatments, such as Fluconazole and Echinocandins [20,21]. Some additional treatment options do exists but they are less favorable due to high costs and toxic effects. In order to prevent further resistance, much more work still needs to be done.

Future Directions

AMR is a natural phenomenon. However, some human actions dramatically accelerate the speed of AMR such as, misuse of antimicrobial drugs and poor attempts at disease prevention. In order to restrict AMR further, proper action needs to be taken by involving the whole community. People have to use antimicrobial drugs properly and, at the same time health-care workers and pharmacists can be more selective when prescribing medications. These simple measures may help to minimize the development of new AMR strains. Policy makers, scientists, and industry professionals need to be involved in development of new diagnostics, treatments and vaccines.

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