

## Biochemical Challenges in Combating Antimicrobial Resistance

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### Editorial

Antimicrobial resistance (AMR) is an emerging global health crisis concerning the ability of a microorganism to withstand the inhibiting or killing action of an antimicrobial. AMR develops as a result of inappropriate use of antibiotics (taking antibiotics for viral infections like cold or flu) or not finishing antibiotics that are prescribed. It threatens the effective treatment of an ever-increasing range of infections caused by bacteria, fungi, parasites and viruses. The World Health Organization (WHO) selected antimicrobial resistance as the theme for World Health Day 2011, chanting “combat drug resistance – no action today, no cure tomorrow”. They also produced in 2014, a global report on AMR surveillance that resistance to common bacteria has reached alarming levels in many parts of the world [1]. A previous study revealed that *Aeromonas* species are common inhabitants of aquatic ecosystems. These *Aeromonas* spp. strains showed to be potential reservoirs of antibiotic resistance genes [2]. The rising AMR of *Pseudomonas aeruginosa* isolated from clinical specimens in India became a great concern to public health officials [3]. High AMR was indicated among antimicrobials widely used in veterinary and human medicine with several *Salmonella* isolates exhibiting multidrug resistance, signaling serious implications in the treatment of salmonellosis in both public and animal health [4]. According to a Center for Disease Control and Prevention report, over twenty thousand Americans died from serious infections caused by AMR bacteria each year [5]. These superbugs include *Clostridium difficile* infection, methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococci* and carbapenem-producing *Enterobacteriaceae*. *Enterococci* can acquire new resistance to antimicrobial agents by mutation or acquisition of extrachromosomal DNA, as plasmids or transposons. Due to the various genetic transfer mechanisms they may elicit, *Enterococci* may become important reservoirs for the spread of antibiotic resistance genes [6]. *E. faecium vanA* is the predominant resistance gene among vancomycin-resistant *Enterococci* bloodstream infections of the urinary tract [7].

A recent Gordon Research Conference in the United States of America has defined primarily three challenges facing the field: limitations of high-throughput-screening-driven target-based discovery, regulatory hurdles to the approval of novel antimicrobial agents, and a serious lack of new diagnostic tools [8]. AMR represents one of today's greatest scientific problems that extend beyond human health. Livestock animals are increasingly infected with AMR bacteria, which can be linked to feeding food animals with antimicrobial drugs for growth promotion and disease prevention. Lee and Wakabayashi conducted a series of interviews with senior government staff in twelve countries to assess their awareness of this issue [9]. All countries felt that laboratory capacity was insufficient and legislation was needed to control inappropriate use of antimicrobials in food animals. Maron and co-workers surveyed the antimicrobial use policies of seventeen

political jurisdictions outside of the United States with respect to growth promotion, disease prevention, and veterinary oversight [10]. Data available from Denmark and Sweden suggest that growth promotion use could be restricted without serious production consequences. National surveillance was set up to counteract scientific unknowns and conflicts of interest among all stakeholders from the farm-to-fork food chain [11].

It has been estimated that current antibiotics will be all but useless within the next two decades. The Medical Research Council (MRC) in UK is leading a new initiative of seven research councils to tackle the ever-growing problem of antimicrobial resistance on all fronts [12]. Biologists, designers, economists, engineers, mathematicians, medical researchers, social scientists and vets are being coordinated in a multi-pronged approach to work on the multi-faceted problem. They will be tracking the extent of AMR in air, cattle, food, homes, hospitals, manure, meat, rivers, sea, soil and water. The basic mechanisms of antimicrobial activity were demonstrated to be inhibition of cell walls, damage to cytoplasmic membranes, inhibition of ribosome function, and inhibition of nucleic acid synthesis [13]. Bacteria have developed many mechanisms to overcome the action of antimicrobial agents, involving the modification of target enzymes, prevention of access to the targets, and synthesis of enzymes that destroy the agents. Mechanisms to overcome resistance include modification of antimicrobial agents. The Canadian Antimicrobial Resistance Alliance has launched a website which is an online research portal designed to aid and educate healthcare providers on the escalating issue of antimicrobial resistance [14]. The site provides the most recent antimicrobial resistance data, key publications from evidence-based medical literature, as well as summary content from major conferences and meetings. The mechanisms of action and resistance are made available as educational videos on  $\beta$ -lactams, fluoroquinolones and macrolides [15].

AMR is a deeply debated subject internationally, with various opinions and perceptions. Any decisions taken by governments should be based on the most accurate interpretation of available scientific evidence. Evaluation of the key AMR pathogens that pose new treatment challenges can lead to drug development opportunities. A paradigm shift is needed in how microbiologists and medical researchers approach the global dealing with AMR-related infections. Imipenem is a broad spectrum antibiotic often used when other antibiotics do not work. Antimicrobials of very high importance are drugs of last resort. If infections do not respond to treatment with these antimicrobials, there is nothing more powerful to turn to [16]. Fortunately over 90 per cent of the antimicrobials used in Canadian feedlot cattle are ionophores, categorized as antimicrobials of low importance, which are never used in human medicine. It is highly important to determine whether the antimicrobial resistance genes found in bacteria from the cattle feedlot environment are exactly the

same as those found in sick people. Cluster-funded research in biochemistry and microbiology is contributing to scientifically sound factual understanding on this perceptual issue. New results will underscore the need for further research into the mechanisms that mediate AMR among bacteria and other microorganisms.

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