

Editorial

Emergence of New Antibiotics

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The growing menace of antibiotic resistance is, arguably, the single biggest threat faced by the world's population. However, in May and June 2014 a change in direction has occurred with the announcement of two new antibiotics. The two drugs represent the first new antibiotics to emerge for several years, and both should be available to the medical community by the end of 2014.

Humans face the very real risk of a future without antibiotics. The implications of this are that life expectancy could fall due to people dying from diseases that are readily treatable today. This was the basis of a recent report by the British Royal Pharmaceutical Society titled "New Medicines, Better Medicines, and Better Use of Medicines". The Society has called for new initiatives, to spur on companies to discover new antibiotics, otherwise, the report warns, people will start "dying from simple surgery" [1].

The Society sees the main problem being pharmaceutical companies not developing new antibiotics. The report argues that pharmaceutical firms tend to make drugs for more profitable, long term conditions. The Society argues the only way forwards as government investment, to give the pharmaceutical companies incentives to develop new antibiotics.

The Royal Pharmaceutical Society was issued around the same time as a major report from the World Health Organization (WHO) about the global threat arising from antibiotic resistant bacteria [2].

The WHO report indicates that "resistance is occurring across many different infectious agents" but the primary focus of the report is on "antibiotic resistance in seven different bacteria responsible for common, serious diseases such as bloodstream infections (sepsis), diarrhoea, pneumonia, urinary tract infections and gonorrhoea."

One aspect of the WHO report is with skin infections. WHO notes that antibiotic resistance causes people to be sick for longer and increases the risk of death. For example, people with MRSA (methicillin-resistant

Staphylococcus aureus) are estimated to be 64% more likely to die than people with a non-resistant form of the infection. *Staphylococcus aureus* are estimated to be 64% more likely to die than people with a non-resistant form of the infection. MRSA is a strain of *Staphylococcus* bacteria, associated with common skin and wound infections, that is resistant to methicillin and first-line antibiotics like beta-lactams. Infection is most serious when associated with bloodstream infection. Infections with drug-resistant strains, like MRSA, can be particularly difficult to treat.

Resistance also increases the cost of health care with lengthier stays in hospital and more intensive care required. This one aspect has seen a step-forward in relation to the unveiling of two new antibiotics.

The first of the new antibiotics is called Dalvance. This is an intravenous drug that can treat skin and soft tissue infections. Dalvance was approved the U.S. Food and Drug Administration (FDA) towards the end of May 2014 [3]. Dalvance is intended to treat acute bacterial skin and skin structure infections caused by certain susceptible bacteria like *Staphylococcus aureus* (including methicillin-susceptible and methicillin-resistant strains) and *Streptococcus pyogenes*. Under the FDA's Qualified Infectious Disease Product directive, the approval of Dalvance was accelerated.

To evaluate the safety and efficacy of Dalvance, the antibiotic was evaluated in two clinical trials using a total of 1,289 adults with acute bacterial skin and skin structure infections. Participants were randomly assigned to receive Dalvance or the alternative antibiotic vancomycin. Results showed Dalvance was as effective as vancomycin for the treatment of the bacterial skin diseases. Given the growing resistance of different bacteria, notably *S. aureus*, to vancomycin, this development represents a significant step forward [4]. Moreover, in the U.S. there were more than 4.8 million hospital admissions of adults with various types of acute bacterial skin and skin structure infections, from 2005 through 2011 [5]. This number included patients with cellulitis, erysipelas, wound infection and major cutaneous abscess.

The second drug is called Oritavancin. Oritavancin is a lipoglycopeptide with bactericidal activity against Gram-positive bacteria. The drug was the subject of a clinical trial study led by G. Ralph Corey of Duke University, and the success was announced in the June 2014 edition of the journal *The New England Journal of Medicine* [6]. The development came about through advancements in the understanding of the mechanisms of binding to Gram-positive bacteria cell wall layers, especially to the peptidoglycan (PG) layer.

The evaluation of Oritavancin involved a randomized, double-blind trial where adults with acute bacterial skin and skin-structure infections received either a single intravenous dose of 1200 mg of Oritavancin or a regimen of intravenous vancomycin, twice per day over a ten day period. Efficacy was assessed by cessation of spreading or reduction in lesion size, absence of fever, and no need for administration of a rescue antibiotic 48 to 72 hours following administration of Oritavancin. Efficacy outcomes, assessed according to the type of pathogen, including methicillin-resistant *Staphylococcus aureus*, were similar in the two treatment groups. Therefore, as with the Dalvance study, Oritavancin was shown to be equivalent to vancomycin.

With both developments the route of administration is also of interest. Here, the use of one-shot antibiotic infusion could transform the treatment of acute bacterial skin infections and alter how these infections are managed. Skin infections are among the most common reasons that doctors use intravenous antibiotics; however, with currently available drugs several infusions are normally required. Both Dalvance and Oritavancin are effective because they persist in the human body.

Although the emergence of two new antibiotics is promising, and will no doubt save many lives, their emergence represents also highlights the lack of progress in relation to other fields of medicine and how far there is still to go in the battle against bacterial 'superbugs'.

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