

## A COMPREHENSIVE REVIEW ON SUPERBUG -INFECTION

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### Abstract:

The rapid spread and dissemination of the multi-drug resistant bacteria world-wide represents a major public health problem. The development of antibiotics decreased the mortality among the humans and animals leading to a better life expectancy. But the injudicious use of antibiotics has developed antibiotic resistance and leads to development of superbug that is no longer responding to the current antibiotics given for the treatment. In this review article a brief note about the superbug types, etiology and other information regarding superbug are described. Superbug should be considered as a serious issue as it may progress further due to irrational usage of antibiotics. To overcome the challenges of antibiotic resistance /superbug infection, antibiotic compounds with new mechanism approach should be done along with proper use of antibiotics.

**Keywords:** superbug, antibiotic resistance, bacteria.

### Introduction

A superbug is a type of bacteria that, over repetitive exposure to antibiotic drugs, becomes resistant to the drug to the point where the drug is no longer effective, therefore becoming antibiotic resistant. In 2013, the U.S. Centers for Disease Control and Prevention (CDC) estimated that at least two million people each year in the United States contract a superbug related illness, and at least 23,000 of these cases are fatal. Deaths caused by superbugs are more prevalent than those caused by HIV/AIDS. The cause of the superbugs are related to improper antibiotic use.<sup>1</sup> Antibiotics have always been considered discoveries one of the wonder discoveries of the 20<sup>th</sup> century. This is true, but the real wonder is the rise of antibiotic resistance in hospitals, communities, and the environment concomitant with

their use. The extraordinary genetic capacities of microbes have benefitted from man's overuse of antibiotics to exploit every source of resistance genes and every means of horizontal gene transmission to develop multiple mechanisms of resistance for each and every antibiotic introduced into practice clinically.<sup>2</sup>

### Definition

The term superbug refers to microbes with enhanced morbidity and mortality due to multiple mutations endowing high levels of resistance to the antibiotic classes specifically recommended for their treatment, the therapeutic options of these microbes are reduced, and periods of hospital care are extended.<sup>2</sup>

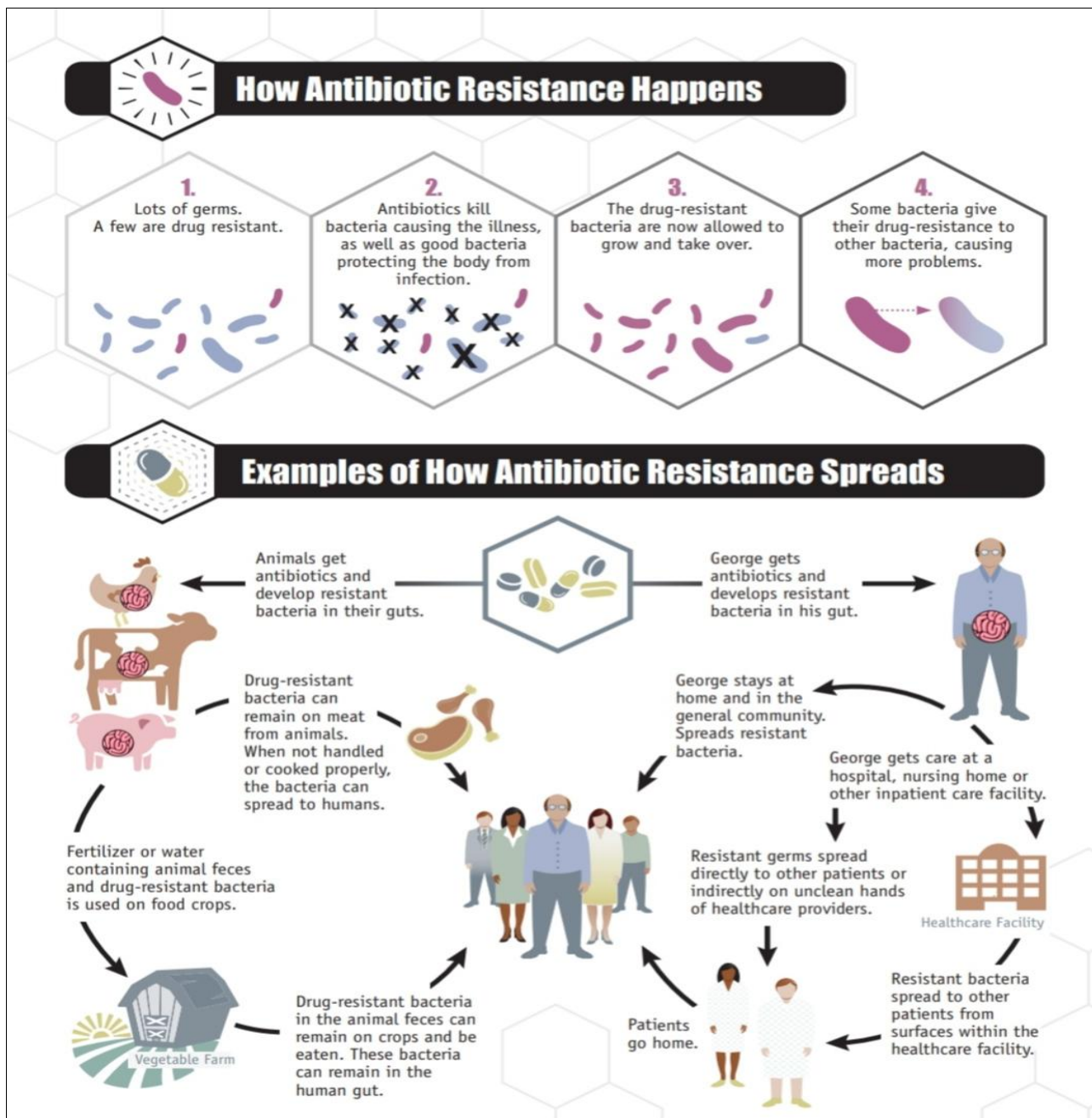
\*Types of superbug infections and minimum estimates of morbidity and mortality from antibiotic-resistance infections<sup>3</sup>

**Table 1: It includes antibiotic-resistant microorganism, infections-included, estimated annual number of cases and estimated annual number of deaths**

Antibiotic-resistant microorganism	Infections included in the case/death estimates	Infections not included	Estimat-ed Annual number of cases	Estimat-ed annual number of deaths
Carbapenam-resistant Enterobacteriaceae (CRE)	Healthcare-associated infections (HAIs) caused by klebsiella and E.coli with onset in hospitalized patients	Infections occurring outside of acute care hospitals (e.g., nursing homes) Infections acquired in acute care hospitals but not diagnosed after discharge Infections caused by Enterobacteriaceae other than klebsiella and E.coli (e.g., Enterobacter spp.)	9,300	610
Drug-resistant Neisseria gonorrhoea (any drug)	All infections	Not applicable	246,000	<5

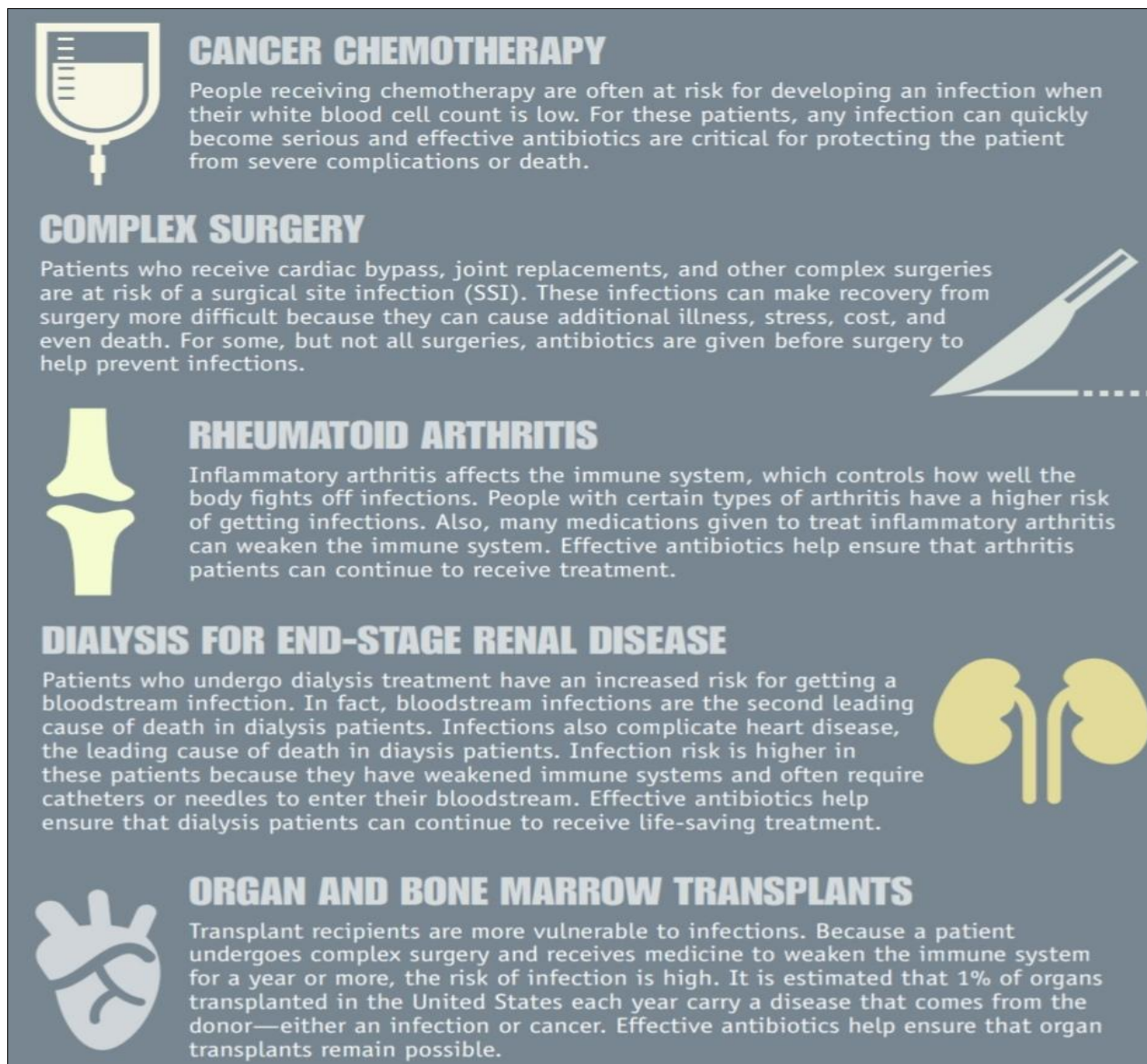
<b>Multidrug-resistant Acinetobacter (three or more drug classes)</b>	HAIs with onset in hospitalized patients	Infections occurring outside of acute care hospitals(e.g.,nursing homes) Infections acquired in acute care hospitals but not diagnosed after discharge	7,300	500
<b>Drug-resistant Campylobacter (azithromycin or ciprofloxacin)</b>	All infections	Not applicable	310,000	28
<b>Drug-resistant Candida (fluconazole)</b>	HAIs with onset in hospitalized patients	Infections occurring outside of acute care hospitals(e.g.,nursing homes) Infections acquired in acute care hospitals but not diagnosed after discharge	3,400	220
<b>Extended-spectrum <math>\beta</math>-lactamase producing Enterobacteriaceae (ESBLs)</b>	HAIs caused by klebsiella and E.coli with onset in hospitalized patients	Infections occurring outside of acute care hospitals(e.g.,nursing homes) Infections acquired in acute care hospitals but not diagnosed after discharge Infections caused by Enterobacteriaceae other than klebsiella and E.coli(e.g.,Enterobacter.spp.)	26,000	1,700
<b>Vancomycin-resistant Enterococcus (VRE)</b>	HAIs with onset in hospitalized patients	Infections occurring outside of acute care hospitals(e.g.,nursing homes) Infections acquired in acute care hospitals but not diagnosed after discharge	20,000	1,300
<b>Multidrug-resistant Pseudomonas aeruginosa (three or more drug classes)</b>	HAIs with onset in hospitalized patients	Infections occurring outside of acute care hospitals(e.g.,nursing homes) Infections acquired in acute care hospitals but not diagnosed after discharge	6,700	440
<b>Drug-resistant non-typhoidal salmonella (ceftriaxone,ciprofloxacin, or 5 or more drugs)</b>	All infections	Not applicable	100,000	40
<b>Drug-resistant salmonella typhi,(ciprofloxacin)</b>	All infections	Not applicable	3,800	<5
<b>Drug-resistant shigella (azithromycin or ciprofloxacin)</b>	All infections	Not applicable	27,000	<5
<b>Methicillin-resistant staphylococcus aureus (MRSA)</b>	Invasive infections	Both healthcare and community-associated non-invasive infections such as wound and skin and soft tissue infections	80,000	11,000
<b>Streptococcus pneumoniae (full resistance to clinically relevant drugs )</b>	All infections	Not applicable	1,200,000	7,000
<b>Drug-resistant tuberculosis (any clinically relevant drug)</b>	All infections	Not applicable	1,042	50
<b>Vancomycin-resistant staphylococcus aureus (VRSA)</b>	All infections	Not applicable	<5	<5
<b>Erythromycin-resistant Group-A streptococcus</b>	Invasive infections	Non-invasive infections including common upper-respiratory infections like strep throat	1,300	160
<b>Clindamycin-resistant Group-B streptococcus</b>	Invasive infections	Non-invasive infections requiring prophylaxis	7,600	440

### Etiology and transmission<sup>3</sup>



**Figure 1: Simply using antibiotics creates resistance. These drugs should only be used to treat infections.**

**People at especially high risk:** As antibiotic resistance grows, the antibiotics used to treat infections do not work as well or at all. The loss of effective antibiotic treatments will not only cripple the ability to fight routine infectious diseases but will also undermine treatment of infectious complications in patients with other diseases. Many of the advances in medical treatment—joint replacements, organ transplants, cancer therapy, and treatment of chronic diseases such as diabetes, asthma, rheumatoid arthritis—are dependent on the ability to fight infections with antibiotics. If that ability is lost, the ability to safely offer people many life-saving and life-improving modern medical advantages will be lost with it<sup>3</sup>.



**Figure 2: It explains about the risk factors for developing superbug infection.**

### **Mechanism of antibiotic resistance**

The prolonged administration or misuse of antimicrobials resulted in selection pressure which favours the evolution of resistant strains and subsequently their transmission causes spread of the resistant strains in the environment. The long-term use of a single antibiotic has favoured the development of strains resistant to both same antibiotics along with other related antibiotics<sup>3</sup>. The spread of resistance traits occurs among different ecological groups and taxonomical groups by the presence of mobile genetic elements like bacteriophage, plasmids, naked DNA, transposonsetc<sup>4-5</sup>. The main resistance mechanisms to

multiple antibiotics in *Acinetobacter* spp. and other superbugs can be summarily outlined as follows (i) production of hydrolyzing enzymes for like  $\beta$ -lactam hydrolysis by different kinds of  $\beta$ -lactamases (Class A to D  $\beta$ -lactamases), (ii) changes in penicillin-binding proteins (PBPs) that prevent the action of  $\beta$ -lactams, (iii) alterations in the structure and number of proteins that result in decreased permeability to antibiotics through the outer membrane of the bacterial cell and (iv) the activity of efflux pumps that further decrease the concentration of antibiotics within the bacterial cell<sup>6</sup>. By Mutation of target sites they resist the action of fluoroquinolones and by modification of

Aminoglycosides by bacterial enzymes they resist Aminoglycosides<sup>7-8</sup> MDR, XTR and TDR TB microorganisms show resistance to antibiotics by spontaneous mutation in various genes<sup>9</sup>. Resistance to Macrolides and related antibiotics mostly occurs due to the r RNA modification responsible for their bindings with ribosomes<sup>10</sup>.

#### Clinical features:

1. Clostridium. difficile infection symptoms: watery diarrhea, Fever, Loss of appetite, Weight loss, Blood or pus in the stool, Increased WBC count, kidney failure
2. MRSA infection symptoms: Small pimple-like bumps that become swollen, red and filled with pus (spider bites)
3. Carbapenem-resistant Enterobacteriaceae infection symptoms: Fever, Chills, Sores that do not heal, Lethargy, Swelling or soreness under the skin<sup>2</sup>

#### Diagnosis and testing

Superbug infection is mainly diagnosed by following ways

- A Sample of infectious skin
- A Sample of pus from a wound
- Blood and urine, sent for Biopsy testing<sup>11</sup>

#### Medication:

Bacterial infections that once succumbed easily to treatment with antibiotics have become highly resistant. In some cases, infections with a superbug can lead to severe disability and death. Some superbugs have developed multi-drug resistance. First line treatments are no longer effective against them.

#### Guidelines for extending the useful lifetimes of antibacterial drugs

- \*Optimal use of antimicrobials
- \*Selective removal, control or restriction of antimicrobial agents or classes
- \*Use of combination antimicrobial therapy to prevent the emergence of resistance.

#### Treatment of MRSA

The antibiotic vancomycin in combination with other intravenous antibiotics such as linezolid and rifampin

remains to be the main treatment for MRSA, however treatment failures attributed to partially resistant bacteria are commonly reported (Bouza, 2009). Drainage of abscesses caused by MRSA is a standard procedure, especially as an adjunct treatment following antibiotic therapy; however, without effective medication therapy this treatment has minimal use. To remain control over MRSA infections, new treatments are regularly developed and tested in clinical settings (Bouza, 2009). Newer treatments which hold promise include second generation glycolipopeptides (such as daptomycin, dalbavancin, and telavancin), the glycylicline class antibiotic tigecycline, and beta-lactam antibiotics (such as ceftobiprole and ceftaroline) (Bouza, 2009)<sup>12</sup>.

#### Prevention and control

Antimicrobial resistant bugs are the emerging present day threats. The followings are some control and preventive measures should be taken to minimize their developments, spread and to promote development of new therapeutics. Most of the infections spread and occur from the contact of infected persons and lack of hygienic practices. Proper sanitation and hygiene maintenance in food and other things can reduce the spread of superbugs. Inappropriate use of antibiotics occurs due to unnecessary length of treatment, wrong prescription and its use without infections<sup>13</sup>. Both physicians and people education about it can check the development of resistant strains. Some policies and regulations should be practiced in both developing and developed countries to check the unnecessary drug promotions<sup>14</sup>. Antibiotics are used vividly in food animals like chicken, cattle, pigs, agricultural fields and fish farming methods. These uses establish a direct link for the appearance of resistance in humans<sup>15</sup>. Attempts should be taken to check the spread of antimicrobial resistances by restricting human to human transmission of resistant strains, decreasing the use of broad spectrum antimicrobial and developing new and novel antimicrobials<sup>16</sup>. Steps should be taken to prevent infections by inhibiting key gene products involved in the infection process<sup>17-19</sup>.

#### CONCLUSION:

Nowadays super bug infections are increasing day by day but there is no simple solution to this problem. Superbug should be considered as serious issues as it

may progress further. The severity of superbug infection, various cause of infection and their preventive measures are discussed in brief in this article. There is no perfect antibiotic, and once the most appropriate uses of any new compound are identified, it is essential that prescription of the antibiotic be restricted to those uses. The physicians and health care centers should provide their patients with antibiotics which are resistance free by taking strict measures in treating infections and controlling the antibiotic use. The exact antibiotics should be used to treat the disease by inhibiting the growth of microorganisms and thus kill them without being further replicating and thus bacterial resistance will be inhibited.

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