



THE EMERGING WORLD OF ANTIBIOTICS AND THE TERROR OF ANTIBIOTIC RESISTANCE MICROORGANISMS: A REVIEW

Leepakshi Dhingra, Pooja Singh, Angkita Sharma, Preeti Arivaradarajan, Shoma Paul Nandi*

*Amity University, Noida, Uttar Pradesh-201313

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Abstract

In today's time many of the pathogenic bacterial strains have started showing resistance to antibiotics which is one of the biggest health challenges faced. This rising popularity gained by pathogens has a propensity to cause infection in people at any phase of life, in healthcare, veterinary, and cultivation industries, enlisting to primary public health challenges, most countries are going to encounter. Antibiotics used inappropriately in human, animals, food, agricultural arenas have caused a rather catastrophic dilemma. Antibiotic resistance results when the bacteria can resist the action of antibiotics and continue causing infection. Both gram-positive and gram-negative resistant bacteria have been deemed serious and urgent threats as they have evolved to develop resistance mechanisms, as a result, the organisms continue to grow and cause infection, even in the presence of antibiotics. In April 2014, World Health Organization (WHO) published the first global report on surveillance of AMR, illustrates the degree of this antibiotic resistance in various parts of the world and also the existence of large breaks in the prevailing investigation, therefore enumerating to be one of the gravest global public health threats in the world.

Keywords

Antibiotics, antibiotic Resistance, pathogenic bacteria, public health challenge, infection.

1. INTRODUCTION

Antibiotics are drugs that are used to destroy or inhibit the growth of bacterial cells. Antibiotics are either bacteriostatic or bactericidal in nature and help the body's immune system to eradicate them [1]. These drugs inhibit the formation of basic genetic material such as the DNA, RNA and hereby inhibiting the protein synthesis too, and this is carried out by many specific actions such as themembrane synthesizing agent.[2] The bactericidal antibiotic is those classes of drugs that kill the bacteria by either interfering with its cell wall synthesis or by inhibiting one of its cell components during replication thus killing it. The bacteriostatic antibiotics are that class that inhibits the further growth of the bacterial infection.

2. Mechanism of action of drugs

The bacteria are targeted by the antibiotics which prevent them from their cell wall and thereby causing cell death. This is because of the presence of a thick peptidoglycan which is present in most of the bacterial cells. The linear strands of peptidoglycan undergo cross-linking due to

transglycosidases, and the peptide chains extend from the sugars present in the polymers, forming the cross-links joining one peptide chain to another.^[5] These sugars are specific derivatives of carbohydrates forming the inside layer of the peptidoglycan layer. The sugar components of the layer contain residues of β -(1,4) linked NAM (N- Acetyl Muramic Acid) and NAG (N- Acetyl Glucosamine) arranged alternatively [3]. These sugars on either side of the layer are joined together with pentapeptides which are cross-linked by the peptide bond that holds them together and thus strengthening the cell wall. These are the antibiotics whose molecular structure consists of a beta-lactam ring. There are various derivatives of beta lactam antibiotics such as penicillin (penams), cephalosporins (cephems), monobactams, carbapenems [4] and carbacephems.

[5] These are the most widely used antibiotics whose action against the bacterial cell is carried out by inhibiting the cell wall synthesis. Protein Synthesis Inhibitors such as tetracycline, erythromycin, chloramphenicol, and

aminoglycosides are the majorly used antibiotics. These antibiotics work as protein-synthesis inhibitors interfering with the cell synthesis and thus inhibiting protein formation. Antibiotics such as erythromycin inhibit the process of protein synthesis by attaching itself to the 23S ribosomal subunit of the 50 S unit and hence prevents the assembly of the various subunits of 50 S ribosomal unit. Erythromycin, clarithromycin and roxithromycin are the antibiotics that inhibit extension at the transpeptidation stage of synthesis by preventing the 50S polypeptide export tunnel.[3]

Replication of all living forms, including bacteria takes place by the replication of the genetic material that is DNA. There is a class of antibiotics that interferes with the replication of DNA by either binding itself to directly one of these or by inhibiting the components of the cell involved in the process of replication and hence the survival. Examples: quinolones, metronidazole, and rifampicin[6]. Quinolones are a primary group of antibiotics that inhibit the process of DNA synthesis by attacking the topoisomerase, the enzyme commonly responsible for the supercoiling of the dsDNA strand, most frequently Topoisomerase II. The topoisomerase II is an instrumental enzyme used in the process involved in the mechanism of DNA replication as it

cuts the double stranded DNA, relaxes the supercoils and then rejoins them together at the cut ends. Therefore, permitting the super coiled strand of DNA to be replicated or even transcribed when they are separate.[7]

Folic acid is a vitamin that is required to make nucleotides and many amino acids. In the absence of an important metabolite like this, the cell would fail to make DNA, RNA and most of the proteins. Bacteria make their own folic acid which is used in many enzymes and many metabolites are formed too. There are certain drugs that inhibit the process of folic acid synthesis that are bacteriostatic because the bacteria cannot reproduce without sufficient folic acid to make DNA, RNA or proteins and broad spectrum as they are effective against various types of bacteria. Different sulpha drugs with the combination of trimethoprim helps in inhibiting different enzymes participating in the mechanism of formation of folic acid. Sulfonamides are competitive inhibitors of dihydrofolate synthesis. Trimethoprim is responsible for inhibiting the action of the enzyme dihydrofolate reductase. When trimethoprim and this enzyme are used together can be used to cure a wide range of susceptible bacterial infections (gram negative and gram positive).[8]

3. Antibiotic Resistance: a concern

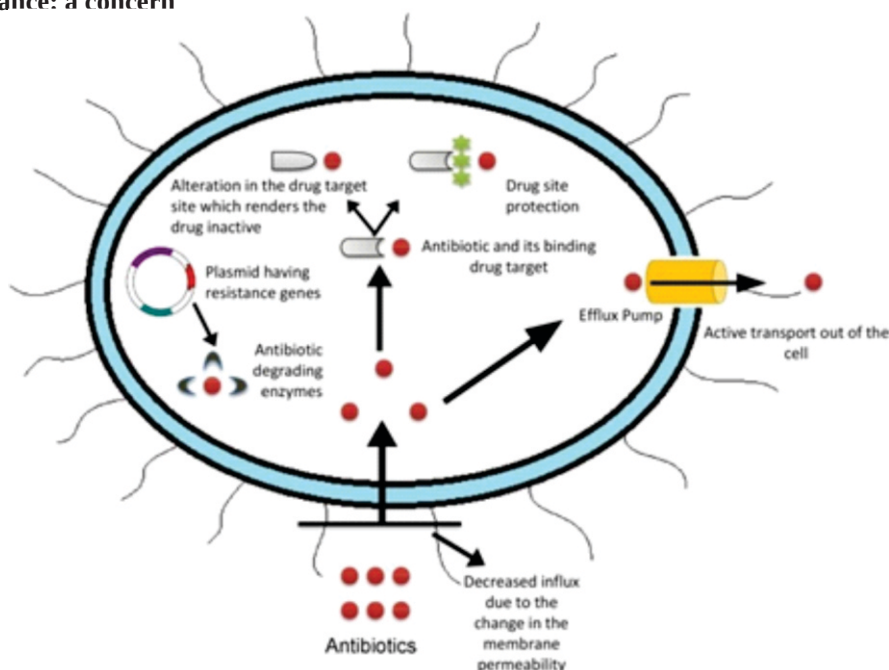


Fig. 1: Showing different resistance mechanisms against antibiotics.

There has been an increase in antibiotic use over the past years, however, the discovery of the various antibiotics has got slow because of the increased resistance of the pathogens against the existing antibiotics. Due to this, the antibiotic which has got resistant to the pathogen/disease is not able to combat the same. The arising resistance of the various microbes including bacteria, viruses, etc. is due to the mutations in their genome that have caused its evolution. This resistance renders our drugs ineffective hence threatening the

most significant advances in medical history. Antimicrobial resistance is posing a serious global threat to the environment, humans and animals.

4. ANTIBIOTIC RESISTANT MICROORGANISMS

- Antibiotic resistant *Gonorrhea* strain
- Metronidazole resistant *Clostridium difficile*
- Methicillin resistant *Staphylococcus aureus*

- ° Vancomycin-resistant *Enterococci* (VRE)
- ° Extended spectrum beta- lactamases (ESBL)
- ° Penicillin resistant *Streptococcus Pneumoniae* (PRSP)
- ° Vancomycin resistant *Staphylococcus aureus* (VRSA)
- ° Multi drug resistant Tuberculosis(MDR-TB)
- ° Multi drug resistant *Staphylococcus Pneumoniae* (MDRSP)

4.1 Antibiotic resistant Gonorrhea strain

Gonorrhea is an infection which is transmitted via sex and spread by the bacteria *Neisseria gonorrhea*. A person is infected with gonorrhea by openings, the bacterial strain entering the body through mouth, anus, penis or vagina. The most common way a woman is infected is by her cervix and the man is mostly infected by the urethra, the tube that carries the urine from the urinary bladder to outside the body. [9]

Mechanism of antibiotic resistance in Gonococcus

Over the past few years, the gonococci bacterial strain has developed tolerance against the action of antibiotic drugs due to the process of mutations and/or gene (whole or parts) acquisition occurring spontaneously, are efficiently chosen because of antibiotic burden in patients and, in the population and generally.[10] On a global scale, this bacteria *N. gonorrhoeae* has shown resistance to almost all significant antimicrobials, including penicillin, quinolones, sulfonamides, macrolides and tetracyclines.[11] This rise of resistance in this bacteria is done by point mutation and also horizontal gene transfer even with other *Neisseria* species. These resistance mechanisms which have been acquired include the alteration in the drug binding site, increased inactivation of antibiotics, decreased concentration of drugs. For example, when there is a mutation in the *penA* gene which is known for encoding the cell wall protein penicillin binding protein 2, confers lesser sensitivity to the beta- lactam drugs [12][13]. The gonococcus strain has known to develop most of the physiological methods of resistance to many antibiotics which are advised during its treatment, e.g., (i) target modification or protection that reduces affinity for the antimicrobials, (ii) modifying or damaging the antimicrobials by enzymatic mechanisms, (iii) increased efflux of antimicrobials, and (iv) decreased influx of antimicrobials. Many genetic determinants responsible for AMR is situated on the chromosomes at the *bla*-TEM gene [14][15] and the *tetM* gene[16]. These genes *bla*-TEM and *tetM* are responsible for causing high resistance to penicillin and tetracycline correspondingly, and this resistance is suspected to be plasmid borne. Gonococci builds its resistance to antibiotics by the process of transfer of genes (transformation and following recombination into the genome) or by means of mutations at specific sites. Introduction of antibiotics to

gonococci or other *Neisseria* spp. for the treatment of gonorrhea or other infections can pick out for strains which inhibit the mechanism of antibiotics.[12]

4.2 Metronidazole resistant *Clostridium difficile*

Clostridium difficile is a gram positive anaerobe causing *Clostridium difficile* infection (CDI) and disrupting the intestinal environment [17]. The most common way of transmitting CDI is by spores and has the capability of causing severe damage to the colon and can be fatal. There has been an increase in the number of deaths by CDI over the past few years and poses an economic burden as well. [18] According to the data given by Centre of Disease Control (CDC), in United States, this infection is responsible for over 29,000 deaths each year with more than 400,000 people getting infected, posing a economic burden of about \$1 billion in additional medical budgetary costs.[19] For the first line of treatment, the antibiotics to be used are metronidazole and vancomycin. Most of the CDI's are susceptible to either of the drugs [20]. The other antibiotics used are erythromycin, clindamycin, penicillins, lincomycin, tetracyclines, aminoglycosides, cephalosporins, and fluoroquinolones, which have been used to treat bacterial infections. [21][22] Metronidazole (MTZ) is a nitroaromatic prodrug with a relatively lower molecular weight and can easily diffuse across the membrane of aerobes and anaerobes as well. [23][23] It has developed multi resistance mechanisms which aids in antimicrobial resistance in *Clostridium difficile*. These resistance mechanisms include the mobile genetic elements (MGEs), genes causing rising resistance in bacterial chromosome, modifications concerning the targets of antimicrobials and/or in absorption ways in *C. difficile*, and in the development of biofilm.[19] Different phenomenon such as conjugation, transduction, or transformation of MEG's specifically transposons within different *C. difficile* strains and other bacterial cells help in acquiring antimicrobial resistance. [21]

A mechanism mediating antibiotic resistance in *C. difficile* includes modifications in the antimicrobial targets and/or in the absorption pathways. Data has been suggested that the rising resistance against Vancomycin might be because of alteration in amino acid constituting the proteins in peptidoglycan biosynthesis like MurG [24] Some different influences like selective pressure due to exposure to antibiotics in the environment make modifications in the objective sites of antimicrobials and/or in the absorption paths in *C. difficile*. For example, due to this method of selective pressure rifampin, rifampin and rifaximin classes of antibiotics, have stopped working against *C. difficile* as they have gained the ability to induce mutations in the sub-unit of the *rpoB* gene, that translates a RNA polymerase of the bacterial strain[25][26]

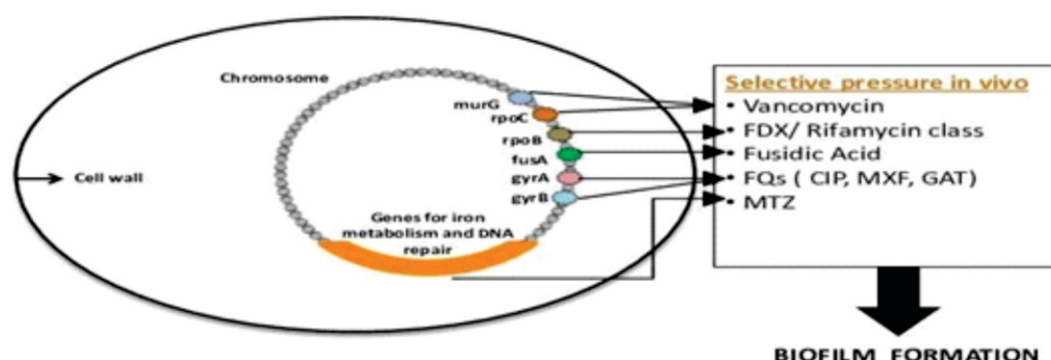


Fig. 2: Selective pressure *in vivo* leading to alterations in antibiotic targets and causes antibiotic resistance. The resistance to the antibiotics also stimulates the bio-film formation. Bio-formation via different mechanisms further contributes to antimicrobial resistance in *Clostridium difficile*. CFs, cephalosporins; CHL, chloramphenicol; CIP, ciprofloxacin; CRO, ceftriaxone; CTT, cefotetan; CTX, cefotaxime; FOX, ceftiofur; FQs, fluoroquinolones; GAT, gatifloxacin; LZD, linezolid; MLSB, macrolide-lincosamide-streptogramin B; MTZ, metronidazole; MXF, moxifloxacin; PBPs, penicillin-binding proteins; TET, tetracycline; VAN, vancomycin.

Formation of biofilm has been found out to be one of the most important factors contributing to antibiotic resistance. The process involving the formation of biofilm involves a dense multicomponent matrix of many layers comprising of DNA, proteins, and polysaccharides. [27] It is evident that biofilms have the ability to defend infective bacteria from adverse stresses which may include antimicrobials and hence promote its survival and virulence. [27]

The mechanism of action of Metronidazole is carried out by its reduction by the pyruvate: ferredoxin oxidoreductase which is commonly present in facultative anaerobic bacteria, and are responsible for alteration in its chemical structure. Pyruvate: ferredoxin oxidoreductase normally triggers the formation of ATP through the process of oxidative decarboxylation of pyruvate. The nitro group in metronidazole while present in the cell acts as an acceptor of electrons which come together and then transfers to the hydrogen ions in the mentioned cycle. The conversion of metronidazole during reduced form is responsible for the creation of a concentration difference that takes up more drugs and stimulates the development of intermediary compounds and free radicals that are lethal to the cell. [23][28][29].

Many studies on the antibiotic resistance in isolates of *C. difficile* from Europe, Asia and North America has reported an increase in resistance to metronidazole as well as to moxifloxacin and clindamycin. [30]

4.3 Methicillin resistant *Staphylococcus aureus*

Staphylococcus aureus is a gram positive bacteria and a usual member of the microbiota of the human body as it is present in the nose of nearly 30% and on the skin of about 20% of the healthy adults. The strength of the ability of aureus to cause infection varies from mild to life threatening. *S. aureus* is known to cause wide range of skin infections and also affects the soft tissues, bones, joints, or it may even cause infection in

the prosthetic devices. [31] According to the data taken from the Emerging Infections Program (EIP) MRSA population surveillance (2005–2016) and the Premier and Cerner Electronic Health Record databases (2012–2017) there is an estimated of 119,247 *S. aureus* bloodstream diseases, with 19832 connected deaths. Although the number of people getting infections has reduced from 2015, there has been a significant morbidity rate with the number of people catching the infections. [32]

The increased resistance in *S. aureus* is primarily due to increased consumption of antibiotics like methicillin and other beta-lactams. Resistance in MRSA is primarily interceded by *mecA* that encodes for a penicillin binding protein PBP-2a that is resistant to the mechanism of action by β -lactams intrinsically [33][34]. When MRSA encounters antibiotics like methicillin, flucloxacillin, dicloxacillin, nafcillin it inactivates the four PBPs present which have a higher-binding-affinity. However, PBP-2a shows a lower binding capacity for methicillin, and then these PBPs, allows the bacterial cell to proliferate in the presence of these antibacterial medicines. PBP 2a is functionally effective in the presence of the different concentrations of β -lactam antibiotics that stops most endogenous PBP enzymes. Then this further takes over for its roles used in the production of cell walls and allows progress in the presence of the β -lactam inhibitors. [35] There are other genes that supervise the phenotype which are methicillin resistant and the PBP-2a production. *MecR1* and *MecI* genes which are situated upstream of the gene *mecA* which are responsible for controlling the PBP-2a expression [36]

4.4 Vancomycin-resistant Enterococci (VRE)

Enterococcus is a gram-positive and anaerobic bacteria which is a common part of the intestinal flora. There are nearly more than 17 different strains but *Enterococcus faecium* and *Enterococcus faecalis* are the most common. Over time enterococcus has developed a resistance

mechanism against a strong antibiotic that was used as a first line therapy to treat it in the first place. A characteristic property of the genus *Enterococcus* is that it confirms resistance to a some amount of antibiotic drugs, even though a few varieties (e.g., *E. faecium*) are further vitally resilient than other species [37]. VRE infections are more difficult to treat than other infections with enterococci, because fewer antibiotics can kill the bacteria [38]. In the past few years, enterococcus not only has been resistant to only vancomycin but also to many beta-lactams and also aminoglycosides[39]. This has led to them becoming the new superbugs which are resistant to many antibiotics, making it difficult to find a cure.

As recognized in the early1950's, when enterococcus was treated with penicillin, the response rate was lower than expected. Later, it was found that most enterococci are resistant to activity of β -lactam and glycopeptide antibiotics inhibiting different bacterial strains[40]. Also, several isolates of *E. faecium* are extremely resistant to penicillins, hence their PBP's have low binding affinity for penicillins.[41]

There are different types of Enterococci resistant to vancomycin that have been categorized based on their phenotypes and genotypes, as summarized in the table 1. [42]

Table 1: Properties of phenotypes of some enterococci resistant to glycopeptides in many reported isolates.[42][43].

Variable	Van A	Van B	Van C	Van D	Van E
Vancomycin MIC ($\mu\text{g/mL}$)	64->1000	4-1024	2-32	64-256	16
Teicoplanin MIC ($\mu\text{g/mL}$)	16-512	≤ 0.5	≤ 0.5	4-32	0.5
Most frequent <i>Enterococcus</i> spp.	<i>E. faecium</i> <i>E. faecalis</i>	<i>E. faecium</i> <i>E. faecalis</i>	<i>E. gallinarum</i> <i>E. casseliflavus</i>	<i>E. faecium</i> -	<i>E. faecalis</i> -
Genetic Determinant	vanA cluster; acquired	vanB cluster; acquired	vanC1, vanC2 cluster; intrinsic	vanD cluster; acquired	vanE cluster; acquired
Transferability	Yes	Yes	No	ND	ND

It was later that vancomycin was proved to be a strong antibiotic and can be used to treat this infection. Vancomycin is an antibiotic of the class glycopeptides that functions when it attaches to the terminal D -Ala- D -Ala. This terminal molecule is a part of the pentapeptide section of the *N*-acetylglucosamine (NAG)-*N*-acetylmuramic acid (NAM) peptidoglycan (PG) cell wall precursor. [44]

It has been nearly 30 years that vancomycin has been used and without any emergence of marked resistance. [45] However, later resistant isolates were found in England, then in France, followed by Eastern countries of United States.[46] Resistance shown against the glycopeptide antibiotics in *Enterococcus* spp. is controlled by the operon (Van) that is the Vancomycin Resistant operon. The Van operon may possibly be transferred on the plasmid, either chromosomally or extra chromosomally. The Van operon comprises of a response regulator that is *vanS-vanR*; a D -lactate dehydrogenase gene, *vanH*; a D -Ala- D -Ala dipeptidase gene, *vanX*; and a type of variable ligase which has 9 variant genes (*vanA*, *vanB*, *vanC*, *vanD*, *vanE*, *vanG*, *vanL*, *vanM*, and *vanN*) [47]

4.5 Extended spectrum beta- lactamases (ESBL)

Beta-lactams are the class of antibiotics which destroy the bacterial cells by acting on their cell wall. It consists of penicillins, carbapenems, monobactams, cephalosporins. The use of beta lactam antimicrobials is very common to treat bacterial infections mostly caused by gram negative bacteria world wide.[48]

The beta-lactams function by inhibiting the final phase in the process for the formation of peptidoglycan which is carried out by acylation of the transpeptidase. The acylation of these transpeptidases forms cross-links in the peptides producing the peptidoglycan. PBP's are the objective site to where the beta-lactams bind, furthermore this method of binding thus interferes with the last transpeptidation process which causes failure of sustainability and thus death via process like self-digestion. [49]

The gram negative bacteria has been exposed to the beta – lactams persistently causing them to develop resistance by forming an enzyme by mutation called as the beta lactamases that renders the antibiotics inactive and broadening their scope of survival. [50] There has been a surprising rise in the number of beta lactamases and the number has reached 200[51].

The enzymes, beta-lactamases, break down the antibiotic by opening the beta-lactam ring and hence it becomes inactive. The two other enzymes which show a familiar action are of the class plasmid mediated beta-lactamases are TEM-1 and TEM-2. They are present in gram-negative bacteria including Enterobacteriaceae, *Pseudomonas aeruginosa*, *Haemophilus influenzae*, and *Neisseria gonorrhoeae* [52]. ESBL is simply transferred among members of *Enterobacteriaceae* because it is plasmid mediated. The distribution of this resistance applies to beta-lactams and also to other frequently utilized antibiotics such as fluoroquinolones, aminoglycosides, and sulphonamides. [53]

These enzymes hydrolyse the penicillins and some of the narrow spectrum cephalosporins.

4.6 Penicillin resistant *Streptococcus Pneumoniae* (PRSP)

There has been an increased resistance in bacteria which has become non susceptible to antibiotics especially penicillin over the past few years. The studies show that there has been a significant rise in the number of penicillin resistant *Streptococcus pneumoniae* in entire Asia as well as the United States. A gradual increase in the intermediate resistance to penicillin (IRP) has been documented in India since 1995.[54][55]

It has been observed that the affinity of the Penicillin Binding Proteins (PBP's) of the gram negative bacteria to bind with the antibiotics have drastically gone down. The isolates were examined from different parts of the world has demonstrated that the decrease in affinity of these PBPs with the antibiotics is resistance mechanism developed by the gram negative bacteria.[56] The primary resistance mechanism in *Streptococcus pneumoniae* is the alteration in the enzyme targets that are the penicillin-binding proteins (PBPs) for the beta-lactams. There has been observed mutation in the enzyme targets (PBPs) that prove the reduced binding interaction of the beta-lactams to the targetsites. However, mutations at points were chosen in the research laboratory, clinical isolates of *Streptococcus pneumoniae* exhibit a structure like mosaic of the altered genes of PBP, the consequence of interspecies gene transfer and events of recombination.[57] The method of beta-lactam resistance of *S. pneumoniae* includes genetic mutations that modify penicillin-binding protein structure, following a decreased affinity for all beta-lactam antibiotics.[58]

A study conducted by Reynolds *et al.* showed that, certain to antibiotic-resistant pneumococcal pneumonia, resistance caused 32,398 additional outpatient visits and 19,336 extra hospitalizations. This led to \$91 million (4%) in direct medical costs and \$233 million (5%) in total costs.[59]

4.7 Vancomycin resistant *Staphylococcus aureus* (VRSA)

Vancomycin resistant *Staphylococcus aureus* are the strains of *S. aureus* that have gradually developed resistance against the glycopeptides, especially vancomycin. There were experiments conducted to study about the vancomycin resistant genes and it was observed that *E. faecalis* can transfer its vancomycin resistant genes to *S. aureus* by gene transfer.[60].

The rare VRSA strains that has the transposon Tn1546, which is developed vancomycin-resistant *Enterococcus faecalis*. This bacterial strain has been suspected to modify the structure of cell wall and its metabolic processes.[61]

The newly discovered VRSA from isolates with a vancomycin MIC $\geq 100\mu\text{g/ml}$ were discovered in wounds of diabetic patients co-infected by *E. faecalis* and MRSA resistant species. Irrespective of their fundamental variations,

the biochemical processes of VISA and VRSA strains has indicated to reveal several shared features.[61]

Vancomycin functions by attaching itself permanently to the terminal $^{\text{D}}$ -alanyl- $^{\text{D}}$ -alanine of disaccharide-pentapeptide precursors in cell wall, and thus hindering assembly of the bacterial cell wall. Enterococci has evolved to develop resistance to vancomycin by way of substituting lactate instead of the terminal alanine, that has a significantly decreased affinity for vancomycin. [62] Many researches of this coagulase-negative staphylococci resistant to vancomycin have demonstrated that these modified cell wall precursors are produced. This is formed, but small quantities as to be included for the degree of resistance detected. [63] There has been a hypothesis that is yet to be proven, that says these modified cross-links may hinder vancomycin binding to peptides acting as targets.[64]

4.8 Multi drug resistant Tuberculosis (MDR-TB)

Multidrug-resistant TB (MDR-TB) is TB that does not act in response to at least isoniazid and rifampicin, the 2 most powerful anti-TB drugs. In 2012, there were approximately 450,000 new cases and 170,000 deaths because of MDR-TB.[65] India has highest burden of Tuberculosis in the world.[66] Figures published by the Ministry of Health in India says that nearly 3 million new cases of TB occur each year in the country.[66] Tubercle bacilli has a surprisingly high proportion of chromosomal mutation that shows resistance to antibiotics. Latest molecular analysis of some MDRTB strains reckons that the MDR phenotype is a consequence of successive accumulation of individual mutations in distinct genes, not by novel methods due to single mutagenic events.[67] The primary explanation for resistance to antibiotics in MTB is the emerging of different mutations in variety of genes encoding for targets to which drug binds or enzymes responsible got activation of drugs. These mutations occur principally in the manner of SNPs, insertions or deletions and to a less significant extent, significant deletions.[68] The mechanism of antibiotic resistance in TB happens via two mechanisms: (i) resistance which occurs primarily is the transmitted antibiotic resistance takes place when the resistant strains are communicated to a new host, and (ii) the resistance that occurs secondarily or developed resistance to drugs, this happens via gaining of drug resistance mutations to single or supplementary drugs. [69][70]

4.9 Multi drug resistant *Staphylococcus Pneumoniae* (MDRSP)

The staphylococcal infections has caused a major concern by showing various antibiotic resistance medication of infections particularly of methicillin-resistant *S. aureus* (MRSA). This has arisen due to the widespread usage of antimicrobial agents, combined with the spread of an significant percentage of the organism by person-to-person contacts.[71]

Conclusion

This is an undeniable fact that the problem of antibiotic resistance has a severe impact on the global health and the

economy of the world altogether. This problem cannot be attained by the combined efforts of the government, the medical professionals and most importantly the public. Before the government talks about the science behind the resistance, it is necessary to create awareness among the public by effective communications, discussions, seminars etc., discussing the harmful effects it has on the society. The concept of properly taking antibiotics and in proper dosage should be inculcated and the harmful effects of resistance to the body should be taught among the people. Apart from the groundwork and interaction with the public, the researchers should take up more research work in the field of AMR, finding the ways with which one can know and develop strategies to combat AMR.

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