Antibiotics and Preventing their Misuse
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Antibiotics are neither like candies, as a layman might think, that can be taken for simple ailments without any medical supervision, nor are they ghostly or deadly substances that one should not even go near to, so much so that one would be scared to take them when prescribed in given medical conditions. They lie somewhere in between where their use need controlled medical supervision.

It is due to the unprecedented increase in the cost of medical treatment, complicated procedures, and unavailability of social medical insurance, more so in the developing and underdeveloped countries, the self medication is on the rise. The other reasons for self medication could be like, easy access to antibiotics without prescription, friend referral, in repeat infections people feel safe to use the same antibiotics prescribed earlier by their doctor and the busy lifestyle that limits people to take an appointment with the doctor etc. While this on one hand poses risk of mistreatment of the medical condition associated with serious side effects, on other hand it has resulted in the widespread resistance to wide range antimicrobial agents. The misuse of antibiotics has been from the medical practitioners too who may prescribe antibiotics just to give a patient feeling of satisfaction that he has been treated well. The high speed trade of unrestricted use of drugs has also encouraged the illegal businesses involving manufacture and marketing of low grade and even fake drugs that puts the lives of genuine patients at risk.

What is an Antibiotic?
Antibiotics are natural substances or chemical compounds that kill bacteria or inhibit their growth [1]. They belong to a broader group of antimicrobial agents, used to treat infections caused by microorganisms, including fungi and protozoa. The word "antibiotic" means any substance produced by a microorganism that inhibits the growth of other microorganisms [2]. Due to the advanced research and development in the medicinal chemistry a large group of antibiotics are now semi synthetic that are modified chemically from original compounds found in nature [3], like beta-lactams (which include the penicillins, produced by fungi in the genus penicillium, the cephalosporins, and the carbapenems). A number of antibiotics are still produced and isolated from living organisms, such as the aminoglycosides. The antibiotics like the sulfonamides, the quinolones, and the oxazolidinones are created through purely synthetic means. Antibiotics can be grouped into following categories:

A-on the basis of their source
1. Synthetic Antibiotics
2. Semisynthetic Antibiotics
3. Natural Antibiotics

B-on the basis of their action
1. Bacteriostatic, and
2. Bactericidal

Antibiotics having lethal action against bacteria are called bactericidal whereas those that prevent bacterial growth are called bacteriostatic. The bactericidal activity of antibiotics may be growth phase-dependent, and, in most but not all cases, the action of many bactericidal antibiotics require ongoing cell activity and cell division for the drugs to kill the bacteria [4]. The activity of antibiotics may be either concentration-dependent or time-dependent.

In concentration dependent types the antimicrobial activity increases with progressively higher antibiotic concentrations. In case of time-dependent antibiotics the antimicrobial activity does not increase with increasing antibiotic concentrations; however, it is important that a minimum inhibitory serum concentration is maintained for a certain length of time [5]. A laboratory evaluation of the killing kinetics of the antibiotic using kill curves is useful to determine the time- or concentration-dependence of the Antibiotic [6].
Depending on their mechanism of action, chemical structure, or spectrum of activity, the antibiotics are classified into various groups and it is very common way of classifying them. Most antibiotics target bacterial functions or growth processes [7]. Antibiotics like (penicillins, cephalosporins), target the bacterial cell wall or cell membrane (polymixins), or interfere with essential bacterial enzymes (quinolones, sulfonamides) and such antibiotics are usually bactericidal (terminating /killing the microorganism) in nature. The other antibiotics such as the aminoglycosides, macrolides, and tetracyclines, that target protein synthesis, are usually bacteriostatic (stopping the further bacterial multiplication and growth) [8].

Antibiotics are further categorized on the bases of their target specificity, i.e; Broad-spectrum antibiotics and Narrow-spectrum antibiotics. The former (broad spectrum) target both Gram positive as well as Gram negative bacteria whereas the latter (narrow spectrum) target either Gram-negative or Gram-positive bacteria.

Side effects

Although antibiotics are considered, in general, safe and well-tolerated, yet they are associated with a wide range of adverse effects [9]. These side-effects may vary. These can be minor or very serious depending on the antibiotics used and the microbial organisms targeted. Side effects can range from fever and nausea to major allergic reactions including photodermatitis and anaphylaxis. Diarrhea, one of the more common side-effects is sometimes caused by the anaerobic bacterium Clostridium difficile, which results from disrupting the normal balance of the intestinal flora, by the antibiotic [10]. The disruption of the population of the bacteria, normally present as constituents of the normal vaginal flora, may occur, and may lead to overgrowth of yeast species of the genus Candida in the vulvo-vaginal area [11]. The other side-effects include elevated risk of tendon damage that results from interaction of antibiotics with other drugs, such as from administration of a quinolone antibiotic with a systemic corticosteroid. Permanent hearing loss can occur when certain antibiotics are administered intravenously, e.g. Aminoglycosides, Vancomycin [12]. In Alcoholics certain antibiotics, including Cephemandole, Cefaperazone Furazolidone, Metronidazole, and Tinidazole, lead to serious side-effects, that include severe vomiting, nausea, and shortness of breath as alcohol interacts with such antibiotics and cause inhibition of metabolism. Alcohol consumption while taking such antibiotics is, therefore, prohibited [13]. Alcohol increases the thickness of peritoneal wall and thereby reduces the absorption of antibiotics. Other effects of alcohol involve the activity of liver enzymes, which break down the antibiotics [14]. Antibiotics like doxycycline and Erythromycin succinate are bacteriostatic and require a sustained level of the drug in the body to be effective. In certain conditions their serum levels may be significantly reduced by alcohol consumption [15]. Increased metabolism and clearance would result in diminished pharmacotherapeutic effect. Alcohol can interfere with the activity or metabolization of antibiotics [16].

Antibiotic resistance

Antibiotic resistance is not spontaneous. It is an evolutionary process where the organisms acquire enhanced ability to survive doses of antibiotics that would have previously been lethal to it [17]. Antibiotics like, Penicillin and Erythromycin, which were previously considered and used to be wonder cures, are now less effective because the bacteria have grown more resistant [18]. Antibiotics themselves act as a selective pressure that allows the growth of resistant bacteria within a population and inhibits susceptible bacteria [19]. Spread of antibiotic-resistant bacteria may be slowed down by reduced fitness in bacteria associated with the resistance, which is disadvantageous for survival of the bacteria when antibiotic is not present. Additional mutations, however, may compensate for this fitness cost and aids the survival of these bacteria [20].

The underlying molecular mechanisms leading to antibiotic resistance can vary. The resistance may be intrinsic or acquired. In intrinsic resistance the bacteria inherits resistance due to its genetic makeup [21]. In the process the bacterial chromosome may fail to encode a protein that the antibiotic target and that results in the inefficacy of the
particular antibiotic against the bacterial strain. Acquired resistance is something that comes with the passage of time or over a period of time resulting from mutation/s in the bacterial chromosome or acquisition of extra-chromosomal DNA [21]. Antibiotic-susceptible bacteria have evolved resistance mechanisms that have been shown to be similar to, and may have been transferred to, antibiotic-resistant strains [22,23]. The spread of resistance may be horizontal or vertical. The example of vertical transmission is spread of antibiotic resistance through transmission of inherited mutations from previous generations and that of horizontal transmission is the genetic recombination of DNA [24]. Plasmids are the main carriers of antibiotic resistance between different bacteria. These carry genes that encode antibiotic resistance that may result in co-resistance to multiple antibiotics [24,25]. Since the different genes, with different mechanisms of resistance to unrelated antibiotics are located on the same plasmid, multiple antibiotic resistance to more than one antibiotic is transferred [25]. On the other hand, cross-resistance to other antibiotics within the bacteria results when the same resistance mechanism is responsible for resistance to more than one antibiotic [25].

Superbugs are antibiotic-resistant microorganisms and these contribute to the re-emergence of diseases which are currently well-controlled. For example, cases of tuberculosis (TB) that are resistant to traditionally effective treatments remain a cause of great concern to health professionals. Every year, nearly half a million new cases of multidrug-resistant tuberculosis (MDR-TB) are estimated to occur worldwide [26]. NDM-1 is a newly-identified enzyme that makes bacteria resistant to a broad range of beta-lactam antibiotics [27].

Preventing Antibiotic misuse

The task of preventing/ reducing the incidences of antibiotic misuse has to be multipronged. All the concerned healthcare bodies need to be involved. These include both the public and the private healthcare institutions.

The most important factor for preventing the menace of antibiotic misuse is the implementation of the Law regulating the prescribing and sale of antibiotics in letter and spirit. It means a lot of hard work on the part of the concerned government agencies to see it through.

A poster campaign was launched in US for reducing the antibiotic misuse. Posters were intended for use in doctor’s offices and other healthcare facilities in U.S, from the U.S. Centers for Disease Control and Prevention, read “Get Smart” AND IT warned that antibiotics do not work for viral illnesses such as the common cold. The first rule of antibiotics is try not to use them, and the second rule is try not to use too many of them [28].

Prescribing antibiotics for certain conditions where their use is not warranted is quite rampant in most countries. Certain conditions can cure without antibiotics but still the antibiotics are prescribed to the patients either to satisfy the patient or the medical companies. An incorrect or sub-optimal antibiotic is prescribed or in some cases for infections [9,29]. Therapeutic usage of antibiotics in hospitals has been seen to be associated with increases in multi-antibiotic-resistant bacteria [30].

Multipronged efforts aimed at both physicians and patients can reduce inappropriate prescribing of antibiotics [31]. On doctor’s front; waiting for 48 hours before prescribing any antibiotics, while observing for spontaneous resolution of infections may reduce antibiotic usage, however, this strategy may reduce patient satisfaction [32].

The common forms of misuses of antibiotic include:

- Travelers using antibiotics for prophylactic purpose to prevent an imagined infection.
- Antibiotic efficacy is compromised when the patient’s weight or history of taking other antibiotics is not taken into consideration when prescribing; this can affect the efficacy of an antibiotic prescription,
- Non compliance to the prescribed dosage frequency and duration is one more important factor.
Certain ailments require a person to take enough time off or rest to allow full recovery, failure to do so would lead to ineffective or less effective antibiotic response. These practices may facilitate the development of bacterial populations with antibiotic resistance. Inappropriate antibiotic treatment is another common form of antibiotic misuse. A common example is the prescription and use of antibiotics to treat viral infections such as the common cold that have no effect.

Various U.S organizations are putting a great effort to improve the regulatory laws governing the antibiotic use [29]. Several U.S agencies like the FDA, the NIH, US center for disease control and prevention are coordinating their efforts to tackle the issue related to antibiotic misuse, antimicrobial Resistance [33]. In France a government launched a campaign named "Antibiotics are not automatic" that started in 2002 that led to a marked reduction of unnecessary antibiotic prescriptions, especially in children [34]. In UK, the campaign was targeted towards patients who request their doctors to prescribe them antibiotics for viral infections, believing these would treat viral infections, reading that 'no amount of antibiotics will get rid of your cold', had very good results.

In developing countries although there are laws that prohibit the sale of antibiotics without a doctor's prescription, it is not observed in practice. The sale of antibiotics in the street pharmacies is rampant. You can put your hand on any antibiotic you like. This is one of the major factors contributing to the widespread antibiotic misuse and resulting antibiotic resistance. Imposing fines or putting license on hold for certain period of time, on Pharmacists who are found continuing practice of selling antibiotics without doctor's prescription, will prove to be of great help. The new government regulations obligating all the private sector to insure their employees is a positive step forward. National level campaign educating the general public about the risks of taking antibiotics without a medical supervision could go a long way to reduce the menace of self medication.

References


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Most antibiotics fall into their individual antibiotic classes. An antibiotic class is a grouping of different drugs that have similar chemical and pharmacologic properties. Their chemical structures may look comparable, and drugs within the same class may kill the same or related bacteria. However, it is important not to use an antibiotic for an infection unless your doctor specifically prescribes it, even if it's in the same class as another drug you were previously prescribed. Taking the wrong antibiotic -- or not enough -- may worsen the infection and prevent the antibiotic from working the next time. There are a few over-the-counter topical antibiotics that can be used on the skin. Some products treat or prevent minor cuts, scrapes or burns on the skin that may get infected with bacteria. Antibiotics are prescription drugs that help treat infections. Some of the more common infections treated with antibiotics include bronchitis, pneumonia, and urinary tract infections. However, antibiotics can have side effects such as nausea, cramps, and fever. Learn more about antibiotics and their side effects. Side Effects of Antibiotics: What They Are and How to Manage Them. Medically reviewed by Alan Carter, Pharm.D. Written by University of Illinois. Updated on April 19, 2019. More common side effects.