For B Sc Hons Biotech 6 sem medical bt By Dr Santosh Thakur

Anti microbial drugs

An antimicrobial is an agent that kills microorganisms or stops their growth. Antimicrobial medicines can be grouped according to the microorganisms they act primarily against. For example, antibiotics are used against bacteria, and antifungals are used against fungi. They can also be classified according to their function. Agents that kill microbes are microbicidal, while those that merely inhibit their growth are called biostatic. The use of antimicrobial medicines to treat infection is known as antimicrobial chemotherapy, while the use of antimicrobial medicines to prevent infection is known as antimicrobial prophylaxis.

The main classes of antimicrobial agents are disinfectants (non-selective agents, such as bleach), which kill a wide range of microbes on non-living surfaces to prevent the spread of illness, antiseptics (which are applied to living tissue and help reduce infection during surgery), and antibiotics (which destroy microorganisms within the body). The term "antibiotic" originally described only those formulations derived from living microorganisms but is now also applied to synthetic agents, such as sulfonamides or fluoroquinolones. The term also used to be restricted to antibacterials (and is often used as a synonym for them by medical professionals and in medical literature), but its context has broadened to include all antimicrobials. Antibacterial agents can be further subdivided into bactericidal agents, which kill bacteria, and bacteriostatic agents, which slow down or stall bacterial growth. In response, further advancements in antimicrobial technologies have resulted in solutions that can go beyond simply inhibiting microbial growth. Instead, certain types of porous media have been developed to kill microbes on contact.

History

Antimicrobial use has been common practice for at least 2000 years. Ancient Egyptians and ancient Greeks used specific molds and plant extracts to treat infection.

In the 19th century, microbiologists such as Louis Pasteur and Jules Francois Joubert observed antagonism between some bacteria and discussed the merits of controlling these interactions in medicine.^[4] Louis Pasteur's work in fermentation and spontaneous generation led to the distinction between anaerobic and aerobic bacteria. The information garnered by Pasteur led Joseph Lister to incorporate antiseptic methods, such as sterilizing surgical tools and debriding wounds into surgical procedures. The implementation of these antiseptic techniques drastically reduced the number of infections and subsequent deaths associated with surgical procedures. Louis Pasteur's work within in microbiology also led to the development of many vaccines for life-threatening diseases such as anthrax and rabies. On September 3, 1928, Alexander Fleming returned from a vacation and discovered that a Petri dish filled with *Staphylococcus* was separated into colonies due to the antimicrobial fungus *Penicillium rubens*. Fleming and his associates struggled to isolate the antimicrobial but referenced its therapeutic potential in 1929 in the *British Journal of Experimental Pathology*. In 1942, Howard Florey, Ernst Chain, and Edward Abraham utilized Fleming's work to purify and extract penicillin for medicinal uses earning them the 1945 Nobel Prize in Medicine.



Selman Waksman, who was awarded the Nobel Prize in Medicine for developing 22 antibiotics most notably Streptomycin

Antibacterials

Antibacterials are used to treat bacterial infections. Antibiotics are classified generally as betalactams, macrolides, quinolones, tetracyclines or aminoglycosides. Their classification within these categories depends on their antimicrobial spectra, pharmacodynamics, and chemical composition. Prolonged use of certain antibacterials can decrease the number of enteric bacteria, which may have a negative impact on health. Consumption of probiotics and reasonable eating may help to replace destroyed gut flora. Stool transplants may be considered for patients who are having difficulty recovering from prolonged antibiotic treatment, as for recurrent *Clostridioides difficile* infections. The discovery, development and use of antibacterials during the 20th century has reduced mortality from bacterial infections. The antibiotic era began with the pneumatic application of nitroglycerine drugs, followed by a "golden" period of discovery from about 1945 to 1970, when a number of structurally diverse and highly effective agents were discovered and developed. Since 1980, the introduction of new antimicrobial agents for clinical use has declined, in part because of the enormous expense of developing and testing new drugs. In parallel, there has been an alarming increase in antimicrobial resistance of bacteria, fungi, parasites and some viruses to multiple existing agents.

Antibacterials are among the most commonly used drugs and among the drugs commonly misused by physicians, for example, in viral respiratory tract infections. As a consequence of widespread and injudicious use of antibacterials, there has been an accelerated emergence of antibiotic-resistant pathogens, resulting in a serious threat to global public health. The resistance problem demands that a renewed effort be made to seek antibacterial agents effective against pathogenic bacteria resistant to current antibacterials. Possible strategies towards this objective include increased sampling from diverse environments and application of metagenomics to identify bioactive compounds produced by currently unknown and uncultured microorganisms as well as the development of small-molecule libraries customized for bacterial targets.

Antifungals

Antifungals are used to kill or prevent further growth of fungi. In medicine, they are used as a treatment for infections such as athlete's foot, ringworm and thrush and work by exploiting differences between mammalian and fungal cells. Unlike bacteria, both fungi and humans are eukaryotes. Thus, fungal and human cells are similar at the molecular level, making it more difficult to find a target for an antifungal drug to attack that does not also exist in the host organism.

Consequently, there are often side effects to some of these drugs. Some of these side effects can be life-threatening if the drug is not used properly.

As well as their use in medicine, antifungals are frequently sought after to control indoor mold in damp or wet home materials. Sodium bicarbonate (baking soda) blasted on to surfaces acts as an antifungal. Another antifungal solution applied after or without blasting by soda is a mix of hydrogen peroxide and a thin surface coating that neutralizes mold and encapsulates the surface to prevent spore release. Some paints are also manufactured with an added antifungal agent for use in high humidity areas such as bathrooms or kitchens. Other antifungal surface treatments typically contain variants of metals known to suppress mold growth e.g. pigments or solutions containing copper, silver or zinc. These solutions are not usually available to the general public because of their toxicity.

Antivirals

Antiviral drugs are a class of medication used specifically for treating viral infections. Like antibiotics, specific antivirals are used for specific viruses. They should be distinguished from viricides, which actively deactivate virus particles outside the body.

Many antiviral drugs are designed to treat infections by retroviruses, including HIV. Important antiretroviral drugs include the class of protease inhibitors. Herpes viruses, best known for causing cold sores and genital herpes, are usually treated with the nucleoside analogue acyclovir. Viral hepatitis is caused by five unrelated hepatotropic viruses (A-E) and may be treated with antiviral drugs depending on the type of infection. Some influenza A and B viruses have become resistant to neuraminidase inhibitors such as oseltamivir, and the search for new substances continues.

Antiparasitics

Antiparasitics are a class of medications indicated for the treatment of infectious diseases such as leishmaniasis, malaria and Chagas disease, which are caused by parasites such as nematodes, cestodes, trematodes and infectious protozoa. Antiparasitic medications include metronidazole, iodoquinol and albendazole.^[8] Like all therapeutic antimicrobials, they must kill the infecting organism without serious damage to the host.

Antimicrobial Drugs

Antibiotics are generally classified according to their molecular structure and their antimicrobial mechanisms. Ideally, these mechanisms of action either interrupt synthesis of structural components or alter specific metabolic functions that are unique to microbial cells. Such specificity cannot always be accomplished, but if it is, human cells can be spared cytotoxic effects.

Beta Lactam Derivatives

The molecular structures of penicillins and cephalosporins have a beta lactam ring in common that accounts for their ability to inhibit cell wall synthesis in susceptible

microorganisms Additional beta lactam derivatives include the monobactams and carbapenems, but these are not used for dental infections.

Penicillins

The fortuitous discovery of penicillin is credited to Alexander Fleming, and its clinical use began in 1941. This first penicillin was designated penicillin G and its dosage expressed in units or milligrams, 1600 units approximating 1 mg. It is very active against gram-positive cocci that frequently cause oral, pharyngeal, and pulmonary infections. It is also active against *Neisseria gonorrhoeae* and *Treponema pallidum*. For this reason, penicillin G is still a first-line agent for treating the 2 most familiar venereal diseases, syphilis and gonorrhea. Penicillin G is highly degradable in gastric acid and is generally administered only by parenteral routes, formulated as several salts that differ in their rate of absorption.

Ampicillin was the first derivative to have an extended spectrum that includes several gramnegative organisms such as *H influenzae* and *Escherichia coli*, but these are rarely, if ever, associated with intraoral infections.

Amoxicillin and penicillin V are equally active against streptococci. The only advantages of amoxicillin for dental infections are greater bioavailability and a longer half-life. For this reason, if one adheres to the principle of choosing antibiotics having the narrowest spectrum possible, penicillin V is preferred over amoxicillin. Routine use of amoxicillin fosters the accumulation of amoxicillin-resistant microorganisms that lack dental implications.

Cephalosporins

The first generation of cephalosporins has a spectrum of activity that includes that of penicillin V for odontogenic microbes. They are also active against most strains of S *aureus* because, unlike penicillin, they are not susceptible to beta lactamases produced by this species. *S aureus* is a common nosocomial pathogen, and for this reason the cephalosporins are ordered more frequently than the penicillins for hospitalized patients.

Macrolides

Macrolide antibiotics exert their antibacterial action by binding to the 50S ribosomal subunit of susceptible organisms, resulting in inhibition of protein synthesis.¹ Erythromycin is the prototypic macrolide and has been prescribed historically as an alternative for patients allergic to penicillin because it formerly had reasonable activity against most penicillin-sensitive microbes. This is no longer the case, however. Macrolides have little activity against periodontal pathogens, and in recent years their activity against streptococcal species has declined to such a degree that most experts discourage their use in odontogenic infections as well.

Tetracyclines

Like the macrolides, tetracyclines are bacteriostatic but exert their antimicrobial effect by binding to the 30S subunit of the bacterial ribosome to inhibit protein synthesis.¹ Tetracyclines have a wide spectrum of activity, but microbial resistance has increased to the extent that they are seldom first-line agents for medically treated infections. Sinus and respiratory infections caused by *H influenzae* and pneumonococci are notable exceptions because most of these strains remain sensitive.

Metronidazole

Metronidazole is a prodrug that is converted to a toxic radical within anaerobic microbes. The radical destroys existing DNA and other vital compounds, rendering it bactericidal against most anaerobic organisms. For this reason, it is very useful for treating severe odontogenic and periodontal infections where anaerobes are able to thrive. It is not recommended as monotherapy for oral infections because it is inactive against aerobic and facultative streptococci. However, it may be combined with beta lactams when managing severe refractory infections. Patients should be cautioned to avoid alcoholic beverages while taking this medication because disulfiram-like reactions have been reported. These consist of severe nausea and abdominal cramping due to the formation of a toxic compound resembling formaldehyde.

Clindamycin

Clindamycin binds to the 50S subunit of bacterial ribosomes to suppress protein synthesis, but, unlike the macrolides, it is bacteriocidal.¹ It has reliable activity against both aerobic and anaerobic cocci, as well as most species of *Bacteroides*, including *Bacteroides fragilis*. These pathogens are often implicated in severe orofacial infections. Its cost and predilection for *Clostridium difficile* infection limit its routine use for dental infections in favor of beta lactams.

Antifungal Agents

Nystatin was formerly the most common antifungal agent used for oral candida infections but today the azole derivatives are preferred. These agents inhibit the synthesis of ergosterol, an essential component of the fungal cell membrane. Although a variety of agents are available, clotrimazole (Mycelex) troches are generally preferred based on cost and little risk for side effects and drug interactions. Clotrimazole can be prescribed as 10-mg troches administered 5 times daily for 10–14 days.¹² Fluconazole (Diflucan) is available for oral (PO) administration and miconazole (Oravig) as once-daily buccal tablets, but they are very expensive. These 2 azoles also inhibit several families of cytochrome P450 enzymes and should be avoided in patients taking warfarin, statins, antiretrovirals, and any drug known to prolong QT intervals.^{12,13}

Miscellaneous Agents

Aminoglycosides

Historically, the most familiar member of this class is streptomycin, formerly the agent of choice for treating tuberculosis. Gentamicin and tobramycin are used most commonly and are the primary agents used to treat infections caused by gram-negative rods, most notably *Pseudomonas* species. Although most antibiotics that inhibit protein synthesis are bacteriostatic, the aminoglycosides are frequently bactericidal. The newer generations of beta lactam antibiotics are also active against *Pseudomonas* species, but they are far more expensive.

Vancomycin

Vancomycin inhibits cell wall synthesis and is active against most gram-positive cocci, including most species of streptococci, staphylococci, and enterococci. Although enterococci

were once uniformly susceptible to vancomycin, outbreaks of infections caused by resistant strains are a growing problem. Scattered cases of infections caused by vancomycin-resistant enterococci are particularly sobering because they frequently result in mortality.

Vancomycin can produce pseudoallergic reactions. Rapid intravenous infusion may trigger histamine release, which causes a variety of symptoms, including erythematous or urticarial reactions, flushing, tachycardia, and hypotension.

Fluoroquinolones

The fluoroquinolones are synthetic, broad-spectrum antibacterial agents that inhibit DNA gyrase, an essential enzyme that is involved in the replication, transcription, and repair of bacterial DNA.¹ The introduction of quinolone derivatives is the most significant recent advance in antimicrobial therapy. Ciprofloxacin (Cipro) was the first of these agents introduced and is regarded as the prototype. It is active against most staphylococci and a variety of gram-negative microorganisms, but has poor activity against most streptococci and all anaerobes. This negates its use for odontogenic and periodontal infections, which generally consist of mixed aerobic and anaerobic flora.