Antibacterial Antibiotics in General Practice

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ABSTRACT

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This detailed review deals with the general aspects of the therapeutics of antibiotics in common use for bacterial infections, with emphasis on those more frequently employed by the family physicians in India.

Since almost all of them are metabolic poisons, they also lead to cellular damage in the host to varying degrees. Therefore adverse side effects are almost universal , the type and severity of the adverse effects varying among the different drugs.

Exposure to antibiotics leads to the proliferation of resistant mutants. This results in ineffectiveness of the drug in the same patients and in those others who get infection from such patients. This problem is probably the most important adverse effect on a community level:

All the common antibiotics used are reviewed.

The antibacterial antibiotic armamentarium is quite well equipped. Judicious selection by the physician is absolutely essential for effectiveness, safety and avoidance of adverse effects. It is also essential that the practicing physician keeps himself abreast of modern developments which aim at fine- tuning the treatment of infective diseases.

Keywords: Antibiotics, Mechanism of action, Adverse effects, Development of antibiotic resistance

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At present antibiotics play a major role in the management of infectious caused by almost all types of microbes. The early part of the twentieth century witnessed the introduction of sulphonamides as specific therapeutic tools against bacterial infections. Introduction of penicillin in the mid part of the 20th century and the success it achieved in curing fatal infections acted as a fillip to formulate newer antimicrobial drugs. The discovery of a multitude of antibiotics, their long term observations – all have led to a subspecialty of "Infectious diseases" in its own right. This specialty deals with the choice of the drug, dosage, duration of treatment, appropriate combinations, identification of adverse effects during and after therapy and several other clinical features which demand very thorough knowledge about the drugs and particular skill for their administration for optimum benefit with minimal adverse effects.

The dictionary meaning of the term antibiotic "is substance capable of destroying or injuring living organisms (eg microbes)". To put it simply, antibiotics are injurious to several living organisms – both small and large. Whereas the microbes succumb to them, the larger organisms escape with minor or even major injury, which may be short-lived or otherwise. The

Table 1. Principal types of antibacterial drugs with their main site of action

Drug	Site of action	mechanisms
Penicillin	Cell wall	Inhibits cell wall synthesis
Cephalosporins	Cell wall	Inhibits cell wall synthesis
Other betalactams	Cell wall	Inhibits cell wall synthesis
Glycopeptides e.g Vancomycin	Cell wall	Inhibits cell wall synthesis
Tetracyclines	Ribosomes	Inhibit protein synthesis
Chloramphenicol	Ribosomes	Inhibit protein synthesis
Aminoglycosides	Ribosomes	Inhibit protein synthesis
Macrolides	Ribosomes	Inhibit protein synthesis
Lincosamides e.gclindamycin lincomycin	Ribosomes	Inhibit protein synthesis
Fusidic acid	Ribosomes	Inhibit protein synthesis
Rifamycin e.g rifampicin	RNA synthesis	Inhibit DNA or RNA synthesis as the case may be
Sulphonamides	Folate metabolism	Inhibit DNA or RNA synthesis as the case may be
Diimidopyrimidines eg, Trimethoprim, pyrimethamine	Folate metabolism	Inhibit DNA or RNA synthesis as the case may be
Quinolones	DNA synthesis	Inhibit DNA or RNA synthesis as the case may be
Nitrofurans e.g nitrofurantoin, nifurtimox	DNA synthesis	Inhibit DNA or RNA synthesis as the case may be
Nitroimidazoles e.g metronidazole, tinidazole	DNA synthesis	Inhibit DNA or RNA synthesis as the case may be

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realm of antibiotics has extended beyond the sphere of microbial infections to other fields such as leukemia and the like. This short review deals with the general aspects of the therapeutics of antibiotics in common use for bacterial infections, with emphasis on those more frequently employed by the family physicians in India.

General considerations

Antibiotics exert their therapeutics effects by acting on the metabolism of microbes at various levels (Table 1).

Since almost all of them are metabolic poisons, they also lead to cellular damage in the host to varying degrees. Therefore adverse side effects are almost universal , the type and severity of the adverse effects varying among the different drugs. The major adverse side effects include:-

1. **Damage to rapidly regenerating cells** – especially gastrointestinal tract, bone marrow, growing foetus etc, manifested as mucusitis of the oral and gastrointestinal mucosa, bone marrow damage leading to varying degrees of hypoplasa and aplasia, foetal abnormalities and the like.

2. **Local effects:** such as gastrointestinal irritation, lesions at injection sites, allergic manifestations - both local and systemic.

3. **Generalized allergic reactions:** leading to acute anaphylactic reaction, delayed serum sickeness-like reaction characterized by fever, anthralgias, skin manifestations and others. Antibiotic–induced fevers may mimic persisting infections and this may be mistaken for continuing infection by the physician.

4. **Consequences of destroying protective microbial flora:** In the skin, gastrointestinal tract, genitourinary tract and other sites overgrowth and even invasion by mildly pathogenic microbes lead to disruption of the mileu interior with worsening of the condition: Eg. antibiotic induced diarrhea, overgrowth of fungal infections, oral and genital ulcerations.

5. **Specific organ toxicity:** These include
   - bone marrow aplasia - eg chloramphenicol
   - neurotoxcity - anti T.B drugs, esp INH
   - damages to growing bones and teeth - tetracyclines.
   - cardiotoxicity - doxorubicin (used in treatment of leukemia)
   - Hepatotoxicity - several antibiotics
   - Fetotoxicity - several antibiotics

6. **Development of microbial resistance:**

Exposure to antibiotics leads to the proliferation of resistant mutants. This results in ineffectiveness of the drug in the same patients and in those others who get infection from such patients. This problem is probably the most important adverse effect on a community level: Classic examples of such resistant organisms include methicillin resistant Staphy coccus aureus (MRSA), multidrug resistant tuberculosis (MDR-TB), extensive resistance of tubercle bacillus (XDR-TB), E coli Pseudomonas, Proteus and others. The problem of bacterial resistance is favoured by prescribing the antibiotics in suboptimal doses and for shorter duration than what is needed for eradication. It is the duty of every physician to take appropriate measures to prevent the development of microbial resistance. Resistance to antibiotics can be minimized (but not abolished completely) by combining them and using them in full doses for the period needed for complete microbial clearance. Since many microbes have developed widespread resistance to antibiotics to which they were originally sensitive, the newer treatment schedules have been modified so as to include antibiotics to which the resistant organisms are still susceptible. Acquisition of resistance by microbes is a very complex process. Organisms may develop resistance when directly exposed to the drug or indirectly by the transfer of genetic material conferring resistance, from other resistant organisms existing in a colony, even without direct exposure to the drug.

The present scenario: The sale of antibiotics exceeds that of any other class of drugs and this contributes to a major share of income and profits of the pharmaceutical industry. Since none of the available antibiotics possess the ideal desirable qualities of prompt effectiveness, absolute safety and prevention of the development of resistance, the therapeutics of antibiotics is undergoing constant change. Previously effective antibiotics have become less effective at present. Eg pencillins for staphylococcus and pneumococcus. INH and rifampicin for M. tuberculosis, chloroquine for P.falciparum malaria and others. As a consequence, continuous pharmacological and pharmaceutical research is going on at a rapid pace to formulate newer and newer antimicrobial drugs and the family physician has to keep abreast of such developments, in order to be up-to-date in professional skills. Moreover the occurrence of many newer infections such as AIDS, variants of influenza virus and hepatitis

viruses, invasive fungal infect ions in immune compromised hosts and others have created the need for introducing newer formulations. Therefore the field of antibiotics is one of the most vibrant part of the pharmaceutical industry. Even though most of the antibiotics were initially isolated from living organisms such as moulds, at present many of them are manufactured by totally synthetic processes

Penicillin's: The basic nucleus is 6–amino penicillanic acid. Further derivatives contain the betalactam ring and all such drugs are included under the common term "betalactam antibiotics". Several microbes have developed resistance to penicillin and betalactam antibiotics by producing betalactamase. Action of penicillin is on the bacterial cell wall and it is bactericidal. Susceptible organisms include gram- positive and gram-negative coccic and gram positive bacteria

Benzyl Penicillin and its derivatives

Benzyl penicillin (Penicillin G) Benzathine penicillin

Procaine penicillin

Phenoxymethyl penicillin (Penicillin V)

Benzyl penicillin (Penicillin G)

Indications: Acute tonsillitis, pharyngitis, otitis media, streptococcal endocarditis, pneumonia, meningococcal and pneumococcal meningitis

Contra Indications: Hypersensitivity to penicillin.

Precaution: History of allergy; renal impairment

Adverse Effects: Anaphylaxis, serum sickness likereactions, Jarisch Herxheimer reaction Paraesthesia with prolonged use, pain at IM injection site, nausea on oral ingestion.

Preparations: Sodium penicillin G (Crystalline Penicillin) 0.5,& 1 MU injection (powder for reconstitution).

Dose: 0.5-5 MU IM or IV 6 – 12 hourly

Since penicillin allergy is widespread and even fatal anaphylactic reaction may occur unexpectedly, it is advisable to give penicillin only after testing for allergy by skin tests. Any history of allergic reaction, even though they are mild, is sufficient reason not to use penicillin.

Benzathine penicillin

Indications: Pharyngitis, prophylaxis of rheumatic fever, syphilis

Contra Indications: As for benzyl penicillin, should not inject intravascularrly

Procaine penicillin

Indications: Should be restricted to organisms that are highly sensitive to penicillin; syphilis; gonorrhoea, anthrax, pneumonia.

Preparations: 0.5 & 1 MU dry powder in vials Dose : Adult – 6-12 lakhs units of procaine penicillin deep IM daily in 1 or 2 divided doses; upto 4.8million units as a single dose given at 2 injection sitesin gonorrhoea.

Phenoxymethyl penicillin (Penicillin V)

Dose : 500mg every 6 hours orally, increase upto750mg in severe infections.

Cloxacillin

Indications: Infections due to penicillinase resistant staphylococci

Preparations: Capsules 250mg, 500mg, Injection 250mg, 500mg as powder for reconstitution and combination preparations with ampicillin in different ratios (tablet, injection, syrup)

Dose: 250-500mg orally 4 times daily half an hour before food; 250mg IM every 4 – 6hours; 500mg slow IV injection every 4-6 hours.

Broad spectrum penicillins

These have broad spectrum antibacterial properties, including action against several gramnegative bacteria. Ampicillin, amoxycillin, piperacillin, ticarcillin and others are included in this group. These can be combined with other antibiotics which increase their activity synergistically (e.g cloxacillin, aminoglycosides) and also substances such as sulbactam, tazobactam and clavulanic acid which inhibit their destruction by the bacterial enzyme, betalactamase. Sulbactam has to be given by injection whereas Clavulanic acid can be given orally.

Antibacterial spectrum includes that of PenicillinG and gram negative bacteria in addition.

Ampicillin

Indications: Urinary tract infection, respiratory tract infection, otitis media, sinusitis, chronic bronchitis, invasive salmonellosis and gonorrhoea.

Contra indications: Penicillin hypersensitivity.

Preparations: Capsules 250mg, 500mg vials for injection 500-1000 mg

Dose: 250 mg to 1g 6 hourly at least 30 minutes before or 2 hours after food; Parenteral dose 500mg/ slow IV every 4-6 hours.

Ampicillin + Sulbactam

Indications: Infections caused by beta lactamase producing organisms.

Preparations: Injection ampicillin 1 g + sulbactam 0.5g
Dose: 1.5 – 3g IV or deep IM 6-8 hourly Ampicillin + Cloxacillin

Indications: Infections caused by beta lactamase producing organisms.

Preparations: Capsule 500mg (250 + 250) Syrup125mg/5ml (30ml)

Dose: 1 cap (250mg ampicillin + 250mg cloxacillin4-6th hourly.

Anoxycillin

Action is similar to that of ampicillin

Combination preparation with cloxacillin or clavulanic acid are available

Dose: 500mg 8th hourly atleast 30 minutes before or 2 hours after food , 500 mg IM or slow IV injection every 4-6 hours

Piperacillin

Indications: Infections due to pseudomonas and klebsiella

Contra indications: As for benzyl penicillin

Precaution: As for benzyl penicillin; renal impairment

Preparations: Injection 1g, 2g and 4g vials;piperacillin + tazobactam is also available .

Dose: 2g 6 hourly or 8 hourly IV

Drug interaction: Piperacillin may inactivate aminoglycosides.

Ticarcillin + Clavulanic acid

Indications: Infections due to pseudomonas and proteus species.

Contra indications: As for benzyl penicillin

Preparations: Injection 1 g vial Dose : 3g IV every 6-8 hours

Cephalosporins

These are synthetic derivatives further developed from the betalactam nucleus. Progress in pharmaceutical manipulation has resulted in the generation of cephalosporins. They have action on gram positive and negative cocci and a multitude of gram negative and gram positive bacilli with slight differences among the members. Depending on their structure and antibacterial spectrum they have been classified into four generations 1 – 4.

First generation cephalosporins

Cephazolin

Indications: Sterilisation of skin prior to surgery; skin and soft tissue tissues infections due to S. aureus and S. pyogenes

Contra indications: Hypersensitivity

Precaution: Penicillin sensitivity, renal impairment

Adverse effects: Skin rash, GI disturbances

Preparations: Injection 500mg and 1 g vial,

Dose: 500mg – 1g IM or IV every 6 -12 hours

Cephalexin

Indications: Upper respiratory tract infection, urinary tract infections and soft tissue infections.

Contra indications: As for cephazolin

Preparations: Capsule 250mg, 500mg

Dose: 1-4 g daily in 4 divided doses Second generation cephalosporins

These have action against anaerobes as well

Cefuroxime

Indications: Upper respiratory tract infections, urinary tract infecti ons and soft tissue infections, meningitis, gonorrhoea and surgical prophylaxis,..

Contra indications: As for cephazolin

Preparations: Injection 250mg, 500mg vial; cefuroxime axetil oral 250 and 500 mg capsules.

Dose: Injection 3g 8h; oral 250mg twice daily

Third generation cephalosporins

These have action against anaerobes also

Cefotaxime

Indications: Cellulitis, meningitis, septicaemia, respiratory and urinary tract infections, intra abdominal infections.

Contra indications: As for cephalexin

Preparations: Injection 250mg, 500mg vials; (cefotaxmine +sulbactam) is also available.

Dose: 1-2g IM or IV 12 hourly.

Ceftriaxone

Indications: Gonorrhoea, enteric fever, meningitis, endo-

carditis, urinary tract infections, lower respiratory tract infections, surgical prophylaxis.

Contra indications: As for cephalexin.

Preparations: Injections 500mg and 1 g (powder for injection)

Dose: For common infections 1g IM or IV daily as a single dose.

For typhoid fever, 4g IV daily in 4 divided doses for 2 days, followed by 2 g daily till 2 days after fever subsides.

Ceftazidime

Indications: Pseudomonal infections like pneumonia, meningitis, septicaemia, respiratory infections, urinary tract infections, skin, soft tissue, bone and joint infections.

Contra indications: As for cephalexin; pain at injection site, rise in liver enzymes.

Preparations: Injection 250 mg, 500mg, 1g(powder for reconstitution)

Dose: 1g IM or IV every 8 hours or 2 g every 12 hours

Cefoperazone

Indications: Infections caused by pseudomonas & bacteroides like urinary tract infections, skin & soft tissue infections, severe respiratory infections, meningitis, septicaemia, gastrointestinal infections.

Contra indications: As for cephalexin; reversible neutropenia

Drug interaction: Disulfiram like reaction with alcohol

Preparations: Injection 250mg, 500mg, 1g

Dose: 1-2g IM or IV every 12 hours

Cefpodoxime proxetil

Indications: Skin and soft tissue infections; respiratory tract infections, urinary tract infections, otitis media, gonorrhoea.

Contra indications: As for cephalexin

Preparations: Tablet 100mg, 200mg

Dose: 200 – 400mg orally 12 hourly

Cefdinir

Indications: Pneumonia, chronic bronchitis, ENTand skin infections.

Contra indications: As for cephalexin

Preparations: capsule 300mg Dose : 300mg twice daily

Cefixime

Indications: Pneumonia, chronic bronchitis, ENTand skin infections.

Preparations: Capsules 200mg, 400mg

Dose: 200 – 400mg orally twice daily Fourth generation cephalosporins

Susceptible Organsisms: Gram negative cocci and bacilli resistant to 3rd generation, gram positive cocci as in 3rd generation; no action on anaerobes.

Cefepime

Indications: Hospital acquired pneumonia, urinary tract infections, intra abdominal infections, septicemia.

Contra indications: Hypersensitivity

Precaution: Severe renal impairment, history of penicillin or cephalosporin allergy.

Adverse effects: Rash , GI disturbances, neutropenia.

Preparations: Injections 1g, 2g (powder for reconstitution)

Dose: 1-2g IV every 12 hours for 7 – 10 days

Cefpirome

Indications: Same as cefipime;

Preparations: Injections 1g vial (powder for reconstitution)

Adverse effects: Taste disturbance shortly after injection

Dose: 1-2g IV or IM every 12 hours

Other betalactam antibiotics

Imipenem + Cilastatin

Indications: Treatment of aerobic and anaerobic gram positive and gram negative infections; surgical prophylaxis; hospital-acquired septicaemia..

Contra indications: Hypersensitivity to imipenem or cilastatin, breast-feeding.

Precaution: Patients known to be hypersensitive to other betalactam antibiotics, renal impairment, CNS disorders, pregnancy.

Adverse effects: Hypersensitivity reactions, GI disturbances, pseudomembraneous colitis, elevation of liver enzymes, Abnormalities in haemotological parameters, positive coomb's test, seizures, taste disturbances, allergic reactions; myoclonus, convulsions, confusion, and mental disturbances; slight increases in liver enzymes and bilirubin rarely hepatitis; increase in serum creatinine and blood urea.

Preparations: Injection, 250mg/ vial, 500mg/vial as

imipenem (powder for reconstitution).

Dose: I.M (as imipenem 500-750 mg, every 12 hours in mild to moderate infections. I.V (as imipenem) 1 – 2g daily in 3-4 divided doses, max,4g or 50mg/kg daily.

Meropenem

Indications: Aerobic and anaerobic gram positive and gram negative infections

Contra indications: Hypersensitivity

Precaution: History of hypersensitivity to other betalactam antibiotics, infants < 3 months, hepatic and renal in sufficiency, neurological disorders, pregnancy, lactation.

Adverse effects: Anaphylaxis, pseudomem- braneous colitis, gastro-intestinal disturbances, pruritus, disturbances in LFT.

Preparations: 500mg and 1 g vial (powder for reconstitution).

Dose: Injection 500 mg – 1 g 8 hourly I.V

Aztreonam

Indications: Hospital acquired infections originating from urinary, biliary, respiratory, gastrointestinal and female genital tracts.

Contraindications: Hypersensitivity, lactation

Precaution: Renal and hepatic impairment;pregnancy.

Adverse effects: Pain and thrombophlebitis at the injection site, seizures

Preparations: 0.5g, 1g, 2g, vials

Dose: 1 – 2g, 6 -8 hourly.

Aminoglycosides

The prototype o this group of drugs was streptomycin discovered by Walksman in the 1950's. Thereafter several drugs in this group have been synthesized and developed. They are mainly effective against gram negative aerobic bacilli such as e.coli, klebisiella, proteun, shigella, proteus, enterobacter and pseudomonas. When combined with betalactam antibiotics, they exhibit synergism. The era of scientific specific treatment of tuberculosis ushered in only with the availability of streptomycin and INH.

Main members in this group are streptomycin, gentamicin, kanamycin, amicacin, netilmycin, neomycin, framycetin and others. They act by inhibiting protein synthesis.

Streptomycin

Indications: It is a bactericidal drug which has to be given by IM injection. Sensitive bacteria include gram negative bacteria, Str viridans, Y pestis, F. tularensis, brucella, M.tuberculosis. It acts synergistically with penicillin for ordinary infections.

Contraindication: Hypersensitivity, renal or hepatic insufficiency, premature infants, pregnancy and myasthenia gravis.

Precaution: Avoid concurrent use of other ototoxic and nephrotoxic drugs.

Adverse effects: Anaohylactic shock. Vestibular dysfunction leading to giddiness and vertigo which may be persistent or even permanent.

Preparations: Injection 0.75g, 1g vial

Dose: 0.75g – 1g IM daily for adults, 15 – 20mg/ kg in children for varying periods for non-tuberculosis infections. In tuberculosis it is used as a second line drug in combination with other drugs for several weeks based on rigid protocols.

Drug interaction: Potentiate nephrotoxicity and ototoxicity produced by other aminoglycosides and cephalosporin, cisplatin, vancomycin. Ototoxicity is potentiated by frusemide. Plasma level will be increased by indomethacin.

Caution: Potentiates the effects of neuromuscular blocking agents administered during anaesthesia

Gentamicin

Indications: Urinary tract infections, pneumonia caused by Pseudomonas aeruginosa, klebsiella, E.Coli or proteus and mycoplasma , meningitis (specially pseudomonas and acinetobacter), peritonitis, enterococcal endocarditis, group A beta haemolytic streptococci and stphylococci.

Contraindication: Pregnancy, lactation and known sensitivity to the drug. Renal insufficiency, myasthenia gravis, hearing disorders

Precaution: Reduce dose in elderly persons and children.

Adverse effects: Nephrotoxicity, irreversible ototoxicity.

Preparations: Injection 40mg /ML 2 mL vials

Dose: Injection 2 – 5 mg/kg IM or IV daily in 3divided doses

Kanamycin

Indications: Used as a second line drug to treat resistant tuberculosis.

Contraindication: Pregnancy, renal failure and hypersensitivity.

Precaution: Breast-feeding. Monitor blood levels when the renal function is impaired.

Adverse effects: Itching, nausea, fever, rash, headache exfoliative dermatitis, neurotoxicity, nephrotoxicity, thrombocytopenia.

Preparations: Injection 0.5g, 1 g vial

Dose: 15mg /kg, 0.5 – 1g IV or IM twice or thrice weekly.

Drug interaction: It potentiates the neuromuscular block by action of muscle relaxants used in anesthesia. May be inactivated by beta-lactam antibiotics. Frusemide increases the nephrotoxicity

Amicacin

This is effective in serious nosocomial gram negative infections, even those resistant to gentamicin and tobramycin. Amicacin is a second line drug for treatment of tuberculosis. The dose is 15mg / kg body weight IM or slow IV in 2 – 4 divided doses daily, the total daily dose not to exceed 1.5 g. Toxicity includes renal damage ototoxicity and inhibition of neuromuscular transmission.

Nctilmycin

This is effective in urinary tract infections, serious systematic infections, even against those resistant to gentamicin. The dose is 4 – 6 mg / kg IM or IV as a single or multiple 8 – 12 hourly injections. In severe infections the dose may be raised to 7.5mg / kg/ day.

Neomycin

This drug is effective locally and hence used for local use in burns, ulcers, and for sterilizing the bowel in hepatic failure and prior to colonic surgery.

Dose for sterilizing the gut – 0.5 – 1g bd orally.

Framycetin

This is used for local antibacterial action in burns, olitis externa, and ocular infections, staphylococcal infections, and to eradicate nasal carriage of staphylococcus.

Tetracyclines

These drugs have been in existence for over six decades. They are bacteriostatic against a wide spectrum of gram negative organisms and gram positive cocci. At present many of these microbes have developed resistance. Due to their bacteriostatic action and the development of microbial resistance they are not used as the first line drugs for organism which are susceptible to the other antibiotics. Still they hold the pride of place for the treatment of rickettsiae, mycoplasma, chlamydia and urea plasma. Their toxicity includes diarrhea hepatic and renal damage, destruction of colonic bacteria leading to nutritional inadequacy, and fetotoxicity Tetracyclines are particularly toxic during pregnancy. The popular currently available preparation is doxycycline.

Dose: 100mg bd orally for 5–10 days or longer. Doxycycline is available as capsules and tablets.

The previously popular preparations were tetracycline, oxytetracycline and chlortetracycline. Dose 250 mg orally 6 hourly for 5 – 7 days. Absorption is better if given on empty stomach. Parenteral dose is 250 – 500mg IM or IV once in8 – 12 hourly.

Macrolides

This name is derived due to the presence of a many-numbered lactone ring in the nucleus. They are effective when given orally. The microbial spectrum includes gram positive cocci, gram negative bacilli, c.diphtheriae, campylobacter, legionella, leptospira, borrelia, nocardia, mycoplasma, and chlamydia, esp Chlamydiatrachomatis. The popular drugs in this class include erythromycin, roxithromycin, azithromycin, clarithromycin and spiramycin.

Table 2. Gives the details for administration

Drug	Dose	Route	Preparation
Erythromycin	250 – 500mg	Oral	Tablets &capsules 100 &500mg
Roxithromycin	150mg bd or300 mg daily	Oral on empty stomach	150 & 300mg capsules
Azithromycin	250 – 500mg	Oral on empty stomach	250 & 500mgtablets, capsules and suspension containing250mg in 5mL
Clarithromycin	250 – 500mg bd or tds	Oral onempty stomach	250 & 500mg tablets
Spiromycin (Rovamycin)	3 millionunits bd for 2– 3 weeks	Oral	Tablets of 3 million units

Note: The macrolides are effective against a large number of organisms. The microbial spectrum is similar to that of penicillin including gram positive and negative cocci, gram positive and gram negative bacilli, acid fast organisms, spirochaetes mycoplasma and Chiamydia trachomatis . They are very effective drugs with a wide margin of safety. They lead to drug interaction when administered concurrently with several other drugs.

Ketolides

The important drug in this class is teilithromycin. Microbial spectrum is similar to that of the macrolides, but more potent than erythromycin. Teilithromycin is active against multidrug resistant pneumococcus, H.influenzae, M.catarrhalis, N.gonorrhoea and N.meningitidis. Dose 800mg oral daily for 7–10 days for community acquired pneumococcus. For others respiratory pathogens the duration is for 5 days. Toxic effects include gastrointestinal upsets hepatic damage, prolongation of Q-T interval in ECG and damage to the mitochondria.

Clindamycin

This drug is highly active against streptococci, pneumococci, (except enterococci), staphylococci (except MRSA) and Corynebacterium acnes B.fragilis, clostridium (except Clostridium difficile) and other anaerobes are usually susceptible.

Indications: Intra abdominal abscess, pelvic abscess, peritonitis, lung abscess, acne vulgaris, malaria, toxoplasma encephalitis, endocarditis, and UTI. It can be used as an alternative to penicillin.

Contraindication: Diarrhoel states.

Precaution: Chronic liver disease, renal disease, pregnancy lactation.

Adverse effects: Diarrhea, pseudomembraneous colitis, skin rash, Stevens Johnson syndrome, hepatic enzyme elevation, granulocytopenia, anaphylaxis, local thrombophelbitis, inhibition neuromuscular transmission, cardiac arrest with rapid IV infusion, oesophageal ulceration.

Preparations: Capsule 150mg Injection 150mg /mL 2ml, 4 ml vials

Dose: Adults – 150 to 300mg 6 hourly up to 450mg every 6 hours in severe infections.

Parenteral: 0.6 – 2.7 g / day IM or IV in 2 – 4divided doses.

Chlormphenicol

A bacateriortatie drug active against gram positive and gram negative organisms, rickettsiae, chlamydia and myoplasma. This drug diffuses well into the CSF and therefore it is very effective for the treatment of meningitis caused by meningococci, pneumococci and H. influenzae. This drug is available as capsules and tablets of 250mg and as injection. Dose is 25 – 50mg / kg bd oral as capsules or tablets in divided doses. Parenteral preparations can be given IV or IM the dosage being the same as oral dose. Till five decades ago it was the first choice for the treatment of salmonella infections, till it fell into disrepute due to widespread resistance developed by salmonellae. Due to the non-use ofchloranphecol in typhoid f ever for a considerable period of time, S.typhi has again become susceptible to chloranphencol.

The drug is toxic to the bone marrow leading to severe and fatal alplastic anima which may occur as a hypersensitivity reaction early in the course of treatment or as a cumulative toxicity when given on long term basis. Due to these dangerous adverse effects, the use of chloranphenicol has come own considerably.

The grey baly syndrome is a toxic state developing in new born infants on exposure to chloramphenicol

Vancomycin

This is a glycopeptide bactericidal antibiotic particularly useful for the treatment of multidrug resistant Staph.aureus and pseudomemebraneous colitis caused by Cl.dificile. It can be given orally and parenterally. It is available as 50mg tablets and vails of 0.5 and 1.g.

Dose: 7mg/kg body weight for pseudo- membraneous colitis.

Oral dose: 125 – 500mg 6 hourly or IV infusion500mg to 1 g given over 1 hour at intervals.

Adverse effects include anaphylaxis, local thrombophlebitis generalized cutaneous rashes, ototoxicity which is partially reversible, sensorineural deafness and nephrotoxicity.

Teicoplanin

This drug is similar to vancomycin in action, but with longer duration of activity. Potentially serious infections by MRSA, infective endocarditis, peritonitis in continuous ambulatory peritoneal dialysis (CAPD) patients and the like demand its use. The drug is available as 200 or 400mg vials for injection.

Dose: 400mg IM or IV loading dose followed by200mg o.d. In severe infections the dose should be doubled. Adverse effects include thrombophlebitis, pruritis, transient eosinophilia and allergic rashes. It is contraindicated during pregnancy and lactation.

Lincomycin

This is a lincosamide antibiotic active against organisms reistant to penicillins. This is particularly useful in the treatment of acute and chronic osteomyelitis,

respiratory infections, septic arthritis and endocarditis. The drug is available as 500 mg capsules and injections containing 600 mg in 2ml.

Dose: 500mg 6 hourly orally or 600mg IV injections every 12 hourly for 10 – 14 days, upto a maximum of 28 days. Adverse effects include diarrhea, headache, lactic acidosis, moniliasis, hypertension, abdominal pain, tongue discoloration, bone marrow suppression with leucopenia and thrombocylopenia, anemia, bleeding, pseudomembraneous colitis, peripheral and optic neuropathy and others.

Rifampicin

It acts by inhibiting the synthesis of nucleic acids. It is bactericidal and sterilizing drug for the treatment of tuberculosis and for the treatment of leprosy.

Contraindications: Hypersensitivity, severe liver disease. thrombocytopenia and acute renal failure are absolute contraindications.

Precautions: Patient should be warned about the orange discolouration of body secretions and urine. It can permanently discolour soft contact lenses otherwise it is harmless.

Along with INH, it is very powerful anti tuberculosis. For tuberculosis the dose is 10mg/kg oral daily, ie 450mg to 600mg daily oral in combination with INH, ethambutol and pyrazinamide. For proper absorption the drug has to be taken on empty stomach and fluid and food are taken only one hour later.

It can also be given for several other non- mycobacterial infections like staphylococci depending upon drug sensitivity

Adverse effects: Flu like syndrome in intermittent dosage, nausea, vomiting, muscle cramps, jaundice, and CNS disturbances, skin reaction, eosinophilia, transient leucopenia, thrombocytopenia, shock, drowsiness, headache, ataxia, visual disturbances and menstrual irregularities.

Available preparations include capsules of 150,300, 450 and 600 mg, tablets 450 – 600 mg and syrup containing 100 mg / 5ml. Rifampicin leads to several drug interactions.

Rifabutin

This is an anti-mycobacterial antibiotic used for the prophylaxis and treatment of M.avium complex.

Dose: 150mg / day oral for six months. In AIDs patients the dose should be 300 mg / day, to be given indefinitely. In MDR tuberculosis, rifabutin can be given in a dose of 300 – 450 mg/ day along with other drugs.

Rifapentine

This is a rifamycin derivative with activity against M.tuberculosis. Since the half life of rifapentine is long compared to rifampicin, this can be given at longer intervals such as 600 mg once a week along with other antituberculosis drugs.

Linezolid

This drug belongs to the class of oxazolidenones, recently synthesised antibiotics which inhibit protein synthesis in bacteria. It is fully absorbed when given orally. It is active against a wide spectrum of gram positive bacteria especially MRSA and vacomycin-resistant Enterococcus faecium.

Dose: 600 mg oral 12 hourly or 600mg IV 12 hourly for 10 – 14 days. Linezolid should not be mixed with other drugs during administration. Adverse effects include pain at injection sites, elevation of liver enzymes, renal impairment and thrombocytopenia.

Daptomycin

This is a cyclic lipoproteid antibiotic that is rapidly bactericidal for most of the gram positive bacteria including Staph.aureus.

Dose: 6 mg / kg body weight given IV once a day.

Spectinoamycin

This drug is active against gonococcus and is the drug choice where penicillin resistance is prevalent.

Dose: 2g IM given as a single dose. Up to 4g can be given IM at two sites simultaneously if a high degree of resistance is suspected. Adverse effects include dizziness, nausea, chills and fever.

Quinupristin – Dalfopristin

This group of drugs belong to the class streptogramins. They are active against gram positive organisms. Vancomycin-resistant MRSA, resistant enterococci and atypical organisms.

Dose: Quinupristin / dalfopristin mixture (30 /70%) is given IV 8-hourly at a dose of 7.5 mg / kg body weight.

Fusidic Acid derivatives

Sodium furidate (fucidin) which has a steroid structure is active against gram positive organisms. All strains of

staphylococci are sensitive, whereas streptococci and pneumococci are relatively resistant.

Dose: 500 – 1000 mg oral, 8-hourly. Milk inhibits absorption of the drug. Parenteral preparation is diethanolamine fusidate. 580 mg IV given, 8-hourly

Fucidin acts synergistically with penicillin and erythromycin. Sodium fusidate is also a general purpose local antiseptic available as ointment.

Other Antibacterial Agents

Sulphonamides

The original sulphonomides have given place to the newer generation derivatives, especially cotrimoxazole - (trimthoprim + sulphamethoxazole) combination. This combination is bactericidal. Being cheap and time tested, this is still popular and widely used

Cotrimoxazole (Trimethoprim + Sulphamethoxazole)

Indications: Acute uncomplicated UTI (except those by enterococci), prevention of recurrent UTI, shigellosis, enteric fever, typhoid carrier state, Pneumocystis Jerovici infection, brucellosis, donovanosis, listeriosis, legionellosis, non tuberculosis mycobacterial skin diseases, pertussis, acute maxillary sinusitis and plague.

Contraindication: Creatinine clearance < 15ml / min, infants < 2 months, pregnancy at term and during lactation.

Precaution: Renal disease, history of hypersensitivity to sulphonamides, patients taking pyrimethamine immunocompromised patients.

Adverse effects: Precipitates megalobastic anemia, leucopenia, thrombocytopenia, exfolitive dermatitis, Stevens Johnson syndrome, toxic epidermal necrolysis, nausea, vomiting, stomatitis, aplastic, haemolytic and macrocytic anemias, coagulation disorders, sulphhaemoglobinaemia, crystalluria.

Preparation: Tablet Sulphamethoxazole 400mg + Trimethoprim 80 mg (regular strength) Tablet Sulphamethoxazole 800 mg + Trimethoprim 160mg (Double strength)

Dose: Acute uncomplicated UTI: single dose treatment 1600 mg sulphamethoxazole + 320 mg Trimethoprim. Prevention of recurrent UTI: trimethoprim + sulphamethoxazole 80/400, od or thrice a week.

Shigellosis: 2 Regular strength tabs bd. For 5 days, To eradicate typhoid carriers state: trimethoprim + sulphamethoxazole 160/800 bd. + rifamycin 400mg/ day, for 6 weeks Pneumocystis Jerovici Infection : Sulpha 100mg / kg / day + Trimethoprim - 20 mg / kg / day in 2 – 3 divided doses for 14 days For Prophylaxis in AIDS. – 1 double strength tab o.d. indefinitely Brucellosis : Along with rifampicin for 8– 12 weeks. Donovanosis : Trimethoprim + Sulphamethoxazola 160 / 800mg bd. Until lesions completely heal. Non-tuberculosis mycobacterial skin diseases : 160 / 800mg bd. For 3 months Pertussis: 8 /40mg / kg /d in 2 divided doses for 2 weeks. Acute maxillary sinusitis: trimethoprim + sulphamethoxazole 160 / 800 b.d for 1 – 2 weeks.

Silversulphadiazine cream 1 % w/w is used as an antimicrobial for preventing infections in burns. Sulphacetamide drops 10%, 20%, and 30% are used for superficial eye infections.

Nitrofurantoin

This is a synthetic nitrofuran possessing bacteriostatic properties used for treating for gram negative bacillary infections, especially in the urinary tract. Tablets of 50 and 100mg are available.

Dose: is 100 mg 6 hourly with meals, for children the dose is 6mg / kg body weight.

Contra indications: renal impairment, previous history of allergy

Adverse side-effects: Headache, exfoliative dermatitis, Stevens Johnson syndrome, aplastic anemia, anaphylaxis, pulmonary fibrosis, hepatitis, hepatic failure, Clostridium difficile associated diarrhea.

Fluro Quinolones

These are very popular and widely available, relatively cheap and very effective anti-bacterial agents which have stood the list of time. They are bactericidal. The parent drug is nalidixic acid.

Antibacterial spectrum includes gram negative cocci and bacilli such as enterobactereciae, H.influnzae, pseudomonas, chlamydia, rickettsiae, legionella, V.cholera and others

They are not active against MRSA and anaerobes. Further refinements of synthesis have given raise to second third and fourth generations of derivatives.

First generation

Ofloxxacin, pefloxacin and lomefloxacin

Second generation

These have better activity against gram positive cocci such as Str pneumoniae and other organisms such as

mycoplasma, legionella and chlamydia. Eg.levofloxacin

Third generation

These have better activity against gram positive cocci such as streptococci, staphylococci, entrococci, M.tuberculosis and mucosa associated infections in AIDS. Eg. Sparfloxacin, gatifloxacin

Fourth generation

Enchanced activity against gram positive organisms and significantly greater activity against anaerobes. Eg.moxifloxacin

Individual members of the fluoroquinolones

First generation fluoroquinolones

Norfloxacin

Indications: Urinary tract infection, genital and GIT infections

Contra indications: Pregnancy, lactation and children < 3 years

Adverse effects: Nausea, epigastric distress, abdominal cramps, rash, anorexia.

Preparations: Tablets 400mg (10)

Ciprofloxacin

Indications: Typhoid and paratyphoid fever, respiratory tract infections, UTI, acute bacterial diarrhea, bone and soft tissue infections, gonorrhoea, anthrax, acute exacerbation of cystic fibrosis with Pseudomonas aeroginosa.

Contraindications: Pregnancy, children < 6 years, allergy

Adverse effects: GI disturbances- anorexia, nausea, vomiting and diarrhea, CNS effects - confusion, agitation, hallucination and convulsions, cartilage damage in young children, leucopenia, allergic reactions, rash, pruritus, photosensitivity.

Preparations: Tablet 250mg and Tablet 500mg Injection 2 mg / ml 100ml Eye drops 0.3 % w/v (5 ml, 10 ml) Eye ointment 0.3 % w/w (5g)

Ofloxacin

Indications: Same as for ciprofloxacin including leprosy

Contra indications: Same as for ciprofloxacin

Adverse effects: Same as for ciprofloxacin, psychotic reactions neuropathy.

Preparations: Tablets 200 mg Tablet 400mgInjection 200 mg

Pefloxacin

Indications: Same as for ciprofloxacin including meningitis

Contra indications: Same as for ciprofloxacin

Preparations: Tablet 200 and 400mg to be taken with meals, Injection 4 mg / 5 ml, to be diluted in100- 250ml of glucose solution but not saline sinceit precipitates in presence of chloride.

Lomefloxacin

Similar to Ciprofloxacin

Preparations: Tablet 400 mg

Dose: 400 mg o.d for 10 – 14 days

Drug interaction: Same as for norfloxacin except that oral iron increases the absorption of lomefloxacin Second generation fluoroquinolones

Levofloxacin

Indications: A/c bacterial sinusitis, a/c exacerbation of COPD, community acquired pneumonia, nosocomial pneumonia, UTI, mycobacterial infections, anthrax, skin & suture infection.

Contraindications: Hypersensitivity, CNS disorders

Adverse effects: GI disturbances, headache, insomnia

Preparations: Tablet of 250mg Tablet of 500mgTablet of 750mg

Dose: 250 -500m g OD Third generation fluoroquinolones

Sparfloxacin

Indications: Community acquired pneumonia, a/c exacerbation of COPD and mucosal infections in AIDS

Contra indications: Hypersensitivity, pregnancy, lactation

Precaution: Slight prolongation of QTc interval. So avoid in patients taking tricyclic antidepressants Class I A and Class III antiarrhythmics

Adverse effects: Same as moxifloxacin

Preparations: Tablet 100mg (6 tab); Tablet 200mg

Dose : 00 – 300mg OD

Gatifloxacin

Indications: RTI, UTI, community acquired pneumonia, sinusitis

Contra indications: Hypersensitivity, age < 18yrs, concurrent use of class IA/II antiarrhythmics,

uncorrected hypokalemia, renal & hepatic impairment.

Precaution: Bradycardia, acute myocardial ischemia, patients with known prolongation of QT interval

Adverse effects: same as in ciprofloxacin + tachycardia, inflammation of tongue/mouth, vaginitis, Hallucinations. Hypo-and hyperglycemia

Preparations: Tablet of 200mg & Tablet of 400mg / Fourth generation fluoroquinolones

Moxifloxacin

Indications: A/c bacterial sinusitis, community acquired pneumonia, skin infection, intra abdominal infection.

Contra indications: Hypersensitivity, age < 18, pregnancy, lactation, bradycardia, heart failure, hypokalemia

Adverse effects: Similar to ciprofloxacin & hematological disturbances, peripheral neuropathy.

Preparation: Tablet of 400mg / Injection 400 mg

Dose: 400mg OD

CONCLUSION

The antibacterial antibiotic armamentarium is quite well equipped. Judicious selection by the physician is absolutely essential for effectiveness, safety and avoidance of adverse effects. It is also essential that the practicing physician keeps himself abreast of modern developments which aim at fine- tuning the treatment of infective diseases.

END NOTE

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