A REVIEW ON TUBERCULOSIS

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ABSTRACT

Tuberculosis is a fatal disease associated with granuloma in different major organs of our body so called as granulomatos disease. The causative agent for the disease is *Mycobacteria tuberculosis* aerobic bacillus bacteria. The disease highly communicable by droplet infection, by using towel, bed seat and by seating near to a patient. The highly effective drugs are available in market but ‘DOT’ the direct observation treatment is used to remove the infection from the body totally. for the patient and to the people around the patient should know about the disease and therapy so that they could follow the precautions to prevent the spreading of infection to nearer people. The present work is an attempt to in torch few aspects of this disease.


INTRODUCTION

Tuberculosis (TB) is a disease of antiquity which is thought to have evolved sometime between the seventh and sixth millennia BC1. Current estimates suggest that one third of the world’s population are infected resulting in some 2 million deaths per year. The 1990 World Health Organization (WHO) report on the Global and expected it to continue in the same position up to 2020. This is deplorable when oneconsiders that various cost-effective tools that can cure tuberculosis have existed since the1960s. TB has the dubious distinction of being the most persistent scourge of humankind2. Worldwide statistics are staggering: in 2001, the WHO estimated that 1.86 billion persons were infected with tuberculosis.
Tuberculosis is a serious but treatable infection, caused by the bacteria *mycobacterium tuberculosis*. It is an acid fast bacillus discovered by Robert Koch, a German scientist in 1882. Three types of bacilli are responsible for tuberculosis in man which include human type, bovine types and atypical or anonymous mycobacteria. The bovine strain affects cattle and other animals.

It is distributed throughout the world but more common in developing countries. Three fourth T.B cases of the world are found in the developing countries and are an important cause of death in most part of the world. It is prevalent both in tropical as well as temperate climates and is more prevalent in large over crowded cities and towns. All domestic animals like cow, buffaloes may suffer from tuberculosis which may sometimes be communicated to man.[1-2]

**STAGES**
- **INFECTION:**—bacteria is alive but body immune system prevent it from spreading. Person is not sick not contagious.
- **ACTIVE DISEASE:**—if immune system is weak bacterium become active and multiplies damage lungs tissues. Person may feel sick may be contagious.

**Types of Tuberculosis**[1-5]

1. Pulmonary tuberculosis.
2. Non pulmonary tuberculosis.

1. **Pulmonary Tuberculosis:**—When mycobacterium tuberculosis cause infection in the lungs it is called pulmonary tuberculosis.
2. **Non Pulmonary Tuberculosis:**—When mycobacterium tuberculosis cause infection in intestine, bones, brain, skin and other parts of the body known as non pulmonary tuberculosis.

**MODE OF SREAD**
It is spread by droplet infection when the droplet are expelled by TB patient through coughing, sneezing, talking and are inhaled by healthy person.

Direct contact with the patient.

By consuming milk derived from a cow suffering from TB and without proper boiling.

By handling sputum and other discharge of TB patient.

By inhaling fine dust particle containing tubercle bacilli derived from dried sputum and other infected discharge throw on floor, walls, clothes etc.

By consuming articles of food and drink contaminated with tubercle bacilli.

Flies play an important role in transmitting the disease by contaminating the articles of food and drink of healthy person with tubercle bacilli.

**INCUBATION PERIOD**

Incubation period varies from a few months to a few year depending upon the host parasite contact and severity of infection.

**Sign and symptoms**
EARLY SYMPTOMS
- A cough that lasts for more than 2-3 weeks.
- Coughing up blood or sputum.
- Weakness or extreme tiredness.
- Loss of appetite.
- Weight loss.
- Night sweats.
- Fever.
- Pain in the chest.

LATER SYMPTOMS
The body is wasted cheeks are flushed eye sunken, and the lips are dry.
The breath has peculiar odour and sputum copious.

RISK FACTOR
A healthy immune system often successfully fight with TB bacteria, but the body can’t mount an effective defense if resistance is low.

- A number of disease weaken immune system include:-
  - HIV/AIDS
  - Diabetes
  - Kidney disease
  - Malnutrition

DIAGNOSIS
- Chest X-ray.
- Tuberculin skin testing.
- Sputum test.
- A CT or MRI scan may be used to look TB in internal organ. For example a brain scan is useful if TB meningitis or TB infection in the brain is suspected.

TUBERCULIN OR MANTOUX TEST[6-10]
This test is performed to find out whether any particular person had any previous tuberculosis infection or not. Sufficient quantity of tuberculin solution is administered intradermally into the skin of the forearm. The site of injection is examined after 72 hrs. The test is considered
positive if there is swelling of at least 6-10 mm in diameter at the site of injection the redness of the skin is no consideration. Reactions less than 6 mm in diameter are considered negative and B.C.G. vaccination is therefore administered preliminary tuberculin testing for newborn infants is unnecessary.

**PREVENTION AND CONTROL**

- One should live in well ventilated house.
- People should be given healthy education.
- One should take nourishing and well balanced diet.
- Milk should be consumed after proper boiling.
- Education and economic condition of people should be raised which will lead to overall improvement in standard of living and sanitary condition.
- Infected person should be isolated.
- While talking or coughing the patient should wear a face mask or keep the handkerchief before his mouth.

**ANTITUBERCULOSIS AGENTS**

Tuberculosis chemotherapy involves giving two to four drugs simultaneously. These drugs work differently so they target the organism in different ways and using a few types of drugs prevents drug resistant strains of Mycobacterium from evolving.

The response of mycobacterial tuberculosis to chemotherapy is slow, and drug must be administered for months depending on which drugs are used. Usually a drug-combination regimen is required for treatment of TB otherwise microbial resistance to any single drug develops rapidly.

Anti-tuberculosis drugs can be divided into two major categories
- First line drug
- Second line drug

**FIRST LINE DRUGS**

Good efficacy, less toxicity and being well tolerated for patients.

- Isoniazid (INH)
- Rifampin
- Pyrazinamide,
- Ethambutol
- Streptomycin.

**ISONIAZID**

Generic and additional names: isonicotinic acid hydrazide; isonicotinylhydrazine, isonicotinylhydrazine; INH; rimitsid; tubazid.

Melting point: 171.4°C

Molecular formula: C₆H₇N₃O

Molecular weight: 137.14

**MECHANISM OF ACTION**

It is *the most active drug for the treatment* of tuberculosis. Isoniazid (INH) is a prodrug activated by catalase-peroxidase hemoprotein, KatG. INH inhibits InhA, a nicotinamide adenine dinucleotide (NADH)-specific enoyl-acyl carrier protein (ACP) reductase involved in fatty acid synthesis. Vilch’eez et al.1 reported that transfer of inhA mutant gene, S94A, into wild-type (WT) *Mycobacterium tuberculosis* was sufficient to confer resistance to INH and ethionamide (ETA), demonstrating that this is the target for INH. INH is a bactericidal agent active against organisms of the genus *Mycobacterium*, specifically *M. tuberculosis*, *M. bovis* and *M. kansasii*. INH is bactericidal to rapidly-dividing mycobacteria, but is bacteriostatic if the mycobacterium is slow-growing. INH is highly specific, being active against only a subset of the mycobacteria and largely ineffective against other microorganisms; this is in part due to several unusual aspects of metabolism, exemplified in *M. tuberculosis*, including unusually high KatG activity and an effective drug efflux mechanism.
INHR recommended for use in pregnancy. As Isoniazid may be associated with an increased risk of hepatotoxicity in pregnant women, symptoms should be assessed, and it is recommended by some that liver function tests be performed fortnightly during the first two months of treatment, and monthly thereafter.

Isoniazid given for treatment of latent tuberculosis (chemoprophylaxis) is considered safe, and is recommended especially where the risk of developing disease is higher, such as with HIV co-infection or with a history of recent contact.

DOSE: 5 mg/kg for adults, 10-20 mg/kg for children.

ADVERSE EFFECT
CNS effects: Peripheral neuropathy is the most common CNS-related toxic effect. It is dose-related, occurs most often in the malnourished and in those predisposed to neuritis (e.g., alcoholics and diabetics), and is usually preceded by paraesthesias of the feet and hands.

Hepatitis: INH does carry a specific warning of the potential for liver toxicity. Liver toxicity and hepatitis risks are increased with concomitant use of carbamazepine, phenobarbital, RIF, and alcohol abuse. Elevated serum transaminase (SGOT, SGPT), bilirubinaemia, bilirubinuria, jaundice, and occasionally severe and sometimes fatal hepatitis can occur with normal dosing regimens. The common prodromal symptoms of hepatitis are anorexia nausea, vomiting, fatigue, malaise, and weakness. Mild hepatic dysfunction, evidenced by mild and transient elevation of serum transaminase levels, occurs in 10-20% of patients taking INH.

Gastrointestinal: effects such as nausea, vomiting, epigastric distress and dark urine can occur but are rare.

Haematological effects: Agranulocytosis; hemolytic, sideroblastic, or aplastic anaemia, thrombocytopenia; and eosinophilia can occur.9Endocrine and metabolic: pyridoxine deficiency, pellagra, hyperglycemia, acidosis and gynecomastia can occur.

Hypersensitivity: Fever, skin rashes, lymphadenopathy and vasculitis can occur.

ADME: It administered orally, well absorbed and widely distributed in body, and metabolized in liver.
Raifpin

**Brand Name:** Rifamycin. Abrifam (Abbott); Eremfat (Fatol); Rifa Rifadin(e), Rifaldin (Aventis); Rifapiam (Piam); Rifaprodin (Almirall); Rifoldin (Aventis); Rimactan(e).

It is a broad spectrum antibiotic. It is a bactericidal for mycobacterium.

**MECHANISM OF ACTION**

Rifampin (RIF) inhibits the essential rpoB gene product β-subunit of DNA-dependent RNA polymerase activity, acting early in transcription. It is thought to bind to the β subunit, close to the RNA/DNA channel, and physically blocks the transit of the growing RNA chain after 2-3 nucleotides have been added. In *Escherichia coli* bactericidal action may come from the triggering of apoptosis via activation of the “suicide gene module” mazEF, and the same system has been identified in *Mycobacterium tuberculosis*. RIF does not inhibit the mammalian enzyme.

During pregnancy Bleeding attributed to hypoprothrominaemia has been reported in infants and mothers following the use of Rifampicin in late pregnancy. The use of Rifampicin is indicated in pregnant women with tuberculosis, with the recommendation that vitamin K be given to both the mother and the infant postpartum if Rifampicin is used in the last few weeks of pregnancy.

RIF has clinical efficacy against a wide variety of organisms, including *Staphylococcus aureus*, *Legionella pneumophila*, Group-A *Streptococcus*, *Brucella spp.*, *Haemophilus influenzae*, and *Neisseria meningitidis*, as well as in vitro activity against penicillin-resistant *Streptococcus pneumoniae*, *N. gonorrhoeae*, *Chlamydia trachomatis*, *H. ducreyi*, and many Gram-negative rods. Due to rapid emergence of resistant bacteria it is restricted to treatment of mycobacterial infections, where the customary use of combination drugs delays resistance development, and the treatment of asymptomatic meningococcal carriers. Efficacy in humans:- Treatment regime most often used: INH, RIF, pyrazinamide (PZA), ETH daily for 2 months followed by INH and RIF 3 times weekly for 4 months.

The drug affects the metabolism of the following drugs: acetaminophen, astemizole, carbamazepine, corticosteroids, cyclosporin, dapsone, ketoconazole, methadone, phenobarbital, phenytoin, quinidine, terfenadine, theophylline, verapamil and warfarin.
Human adverse reactions
Hepatitis and serious hypersensitivity reactions including thrombocytopenia, hemolytic anaemia, renal failure have been reported. Asymptomatic elevations of serum transaminase enzymes, increase in serum bile acids and bilirubin concentrations can occur. Marked elevation of serum alkaline phosphatase and bilirubin suggests RIF toxicity.

Cardiovascular: Hypotension and shock.

Respiratory: Shortness of breath.

CNS: Rare cases of organic brain syndrome have been reported (i.e. confusion, lethargy, ataxia, dizziness and blurring of vision). Peripheral neuropathy, affecting the limbs, muscles and joints in the form of numbness and pain, has been reported.

Gastrointestinal: Nausea, vomiting, diarrhoea. RIF causes orange-red staining of all body fluids.

Human dosage: 300 mg tablets. Dose 10 mg/kg, in a single daily administration, not to exceed 600 mg/day, oral or i.v.

ETHAMBUTOL
Brand names: Aethambutolum, D-Ethambutol, Dadibutol, Diambutol, EMB, Ethambutol HCL, Etibi, Myambutol, Tibutol.

MECHANISM OF ACTION
Ethambutol (ETH) inhibits arabinosyl transferases involved in cell-wall biosynthesis in Mycobacterium smegmatis two polymers seem to be directly affected arabinogalactan (AG) and lipoarabinomannan (LAM). AG forms part of the mucolyl-AG-peptidoglycan layer which anchors the peptidoglycan layer to the lipid-mycolic acid outer layer. LAM appears to be attached to the cell membrane via phosphatidyl-inositol. In M. smegmatis, ETH inhibited synthesis of arabinan completely and inhibited AG synthesis most likely as a consequence of this; more than 50% of the cell arabinan was released from the bacteria following ETH treatment, whereas no galactan was released.

Spectrum of activity: ETH is effective against actively growing microorganisms of the genus Mycobacterium, including M. tuberculosis. Nearly all strains of M. tuberculosis and M. kansasii as well as a number of strains of the M. avium complex (MAC) are sensitive to ETH.
**Efficacy in humans:** ETH is described as “fourth drug” for empiric treatment of M. tuberculosis and M. avium. ETH is used as an adjunct in the treatment of pulmonary tuberculosis especially in cases of suspected drug resistance. ETH should not be used alone due to the real risk of resistant mutants. ETH plus INH or streptomycin.

**Adverse reactions:** The most common toxic effect of ETH is optic neuropathy, generally reversible although irreversible blindness has been reported. Hepatotoxicity has been reported; baseline and periodic assessment of hepatic function should be performed during treatment. Other side effects that have been observed are joint pain, gastrointestinal upset, abdominal pain, malaise, headache, dizziness, mental confusion, disorientation, and possible hallucinations.

**Streptomycin**[^14][^15]

Streptomycin is an antibiotic (antimycobacterial) drug, the first of a class of drugs called aminoglycosides to be discovered, and it was the first effective treatment for tuberculosis. It is derived from the actinobacterium *Streptomyces griseus*. Streptomycin is an abactericidal antibiotic.

Streptomycin is a water-soluble aminoglycoside. It is marketed as the sulfate salt of streptomycin. The chemical name of streptomycin sulfate is D-Streptamine, O-2-deoxy-2-(methylamino)-α-L-glucopyranosyl-(1→2)-O-5-deoxy-3-C-formyl-α-L-lyxofuranosyl-(1→4)-N,N-bis(aminomimonomethyl)-,sulfate (2:3) (salt). The molecular formula for Streptomycin Sulfate is (C\textsubscript{21}H\textsubscript{39}N\textsubscript{7}O\textsubscript{12})\textsubscript{2}·3H\textsubscript{2}SO\textsubscript{4} and the molecular weight is 1457.41.

**Mechanism of action**

Streptomycin is a protein synthesis inhibitor. It binds to the small 16S rRNA of the 30S subunit of the bacterial ribosome, interfering with the binding of formyl-methionyl-tRNA to the 30S subunit. This leads to codon misreading, eventual inhibition of protein synthesis and ultimately death of microbial cells through mechanisms that are still not understood. Speculation on this mechanism indicates that the binding of the molecule to the 30S subunit interferes with 50S subunit association with the mRNA strand. This results in an unstable ribosomal-mRNA complex, leading to a frameshift mutation and defective protein synthesis; leading to cell death. Humans have ribosomes which are structurally different from those in bacteria, so the drug does not have this effect in human cells. At low concentrations, however, streptomycin only inhibits growth of the bacteria by inducing prokaryotic
ribosomes to misread mRNA. Streptomycin is an antibiotic that inhibits both Gram-positive and Gram-negative bacteria and is therefore a useful broad-spectrum antibiotic.

Uses

- Infective endocarditis caused by enterococcus when the organism is not sensitive to Gentamicin
- Tuberculosis in combination with other anti-TB drugs. It is not the first-line treatment, except in medically under-served populations where the cost of more expensive treatments is prohibitive.
- Plague (Yersinia pestis) has historically been treated with it as the first-line treatment. However it is approved for this purpose only by the U.S. Food and Drug Administration.
- In veterinary medicine, streptomycin is the first-line antibiotic for use against gram negative bacteria in large animals (horses, cattle, sheep, etc.). It is commonly combined with procaine penicillin for intramuscular injection.
- Tularemia infections have been treated mostly with Streptomycin and some other antibiotic drugs, which is effective, but the infection is resistant to Penicillin.
- **Pesticide and fungicide:** Streptomycin also is used as a pesticide, to combat the growth of bacteria, fungi, and algae. Streptomycin controls bacterial and fungal diseases of certain fruit, vegetables, seed, and ornamental crops, and it controls algae in ornamental ponds and aquaria. A major use is in the control of fireblight on apple and pear trees. As in medical applications, extensive use can be associated with the development of resistant strains.
- **Cell culture:** Streptomycin, in combination with penicillin, is used in a standard antibiotic cocktail to prevent bacterial infection in cell culture.
- **Protein purification:** When purifying protein from a biological extract, streptomycin sulfate is sometimes added as a means of removing nucleic acids. Since it binds to ribosomes and precipitates out of solution, it serves as a method for removing rRNA, mRNA, and even DNA if the extract is from a prokaryote.

Side effects

- Fever and rashes result from persistent use.
- The vestibulococlear nerve can be affected, resulting in tinnitus, vertigo and ataxia.
- It can also lead to nephrotoxicity and can potentially interfere with diagnosis of kidney malfunctioning.
A.D.M.E:- All of the aminoglycosides are absorbed rapidly from intramuscular sites of injection. Peak concentrations in plasma occur after 30 to 90 minutes and are similar to those observed 30 minutes after completion of an intravenous infusion of an equal dose over a 30 minute period. In critically ill patients, especially those in shock, absorption of drug may be reduced from intramuscular sites because of poor perfusion.

**Pyrazinamide**

Pyrazinamide is a drug used to treat tuberculosis. The drug is largely bacteriostatic, but can be bacteriocidal on actively replicating tuberculosis bacteria.

**Mechanism of action**

Pyrazinamide is a prodrug that stops the growth of *Mycobacterium tuberculosis*.

Pyrazinamide diffuses into *M. tuberculosis*, where the enzyme pyrazinamidase converts pyrazinamide to the active form pyrazinoic acid. Under acidic conditions, the pyrazinoic acid that slowly leaks out converts to the protonated conjugate acid, which is thought to diffuse easily back into the bacilli and accumulate. The net effect is that more pyrazinoic acid accumulates inside the bacillus at acid pH than at neutral pH.

Pyrazinoic acid was thought to inhibit the enzyme fatty acid synthase (FAS) I, which is required by the bacterium to synthesise fatty acids although this has been discounted. It was also suggested that the accumulation of pyrazinoic acid disrupts membrane potential and interferes with energy production, necessary for survival of *M. tuberculosis* at an acidic site of infection. Further studies reproduced the results of FAS I inhibition as the putative mechanism first in whole cell assay of replicating *M. tuberculosis* bacilli which have shown that pyrazinoic acid and its ester inhibit the synthesis of fatty acids. This study was followed by in vitro assay of tuberculous FAS I enzyme that tested the activity with pyrazinamide, pyrazinoic acid and several classes of pyrazinamide analogs. Pyrazinamide and its analogs inhibited the activity of purified FAS I. Pyrazinoic acid binds to the ribosomal protein S1 (RpsA) and inhibits trans-translation. This may explain the ability of the drug to kill dormant mycobacteria.

Mutations in the *pncA* gene, which encodes a pyrazinamidase, is responsible for the appearance of most pyrazinamide resistant *M. tuberculosis* strains. A few pyrazinamidase resistant strains with mutations in the *rpsA* gene have also been identified.
Uses
Pyrazinamide is only used in combination with other drugs such as isoniazid and rifampicin in the treatment of *Mycobacterium tuberculosis*. It is never used on its own. It has no other indicated medical uses. In particular, it is not used to treat other mycobacteria; *Mycobacterium bovis* and *Mycobacterium leprae* are innately resistant to pyrazinamide. Pyrazinamide is used in the first two months of treatment to reduce the duration of treatment required. Regimens not containing pyrazinamide must be taken for nine months or more.

Pyrazinamide in conjunction with rifampin is a preferred treatment for latent tuberculosis.

Pyrazinamide is a potent antiuricosuric drug and consequently has an off-label use in the diagnosis of causes of hyperuricemia and hyperuricosuria. It acts on URAT1.

A.D.M.E
Pyrazinamide is well absorbed orally. It crosses inflamed meninges and is an essential part of the treatment of tuberculosis meningitis. It is metabolised by the liver and the metabolic products are excreted by the kidneys.

Pyrazinamide is routinely used in pregnancy in the UK and the rest of the world; the WHO recommends its use in pregnancy; and there is extensive clinical experience to show that it is safe. In the U.S., pyrazinamide is not used in pregnancy, citing insufficient evidence of safety. Pyrazinamide is removed by haemodialysis and therefore doses should always be given at the end of a dialysis session.

Second-line drugs
Usually used as alternatives to the first-line drug when drug resistance occurs or when a particular therapy is required.

- Para-aminosalicylic acid.
- Kanamycin.
- Amikacin.
- Capromycin.
- Ciprofloxacin.
- Ethionamide.
Para amino salicylic acid

This organic compound has also been use since the 1940s for the treatment of inflammatory bowel diseases (IBDs), where it has shown greater potency in ulcerative colitis and Crohn's disease. It is thought to act via NF-κB (nuclear factor-kappa B) inhibition and free radical scavenging. 5-Aminosalicylic acid, sold under the name mesalazine, is a closely related compound that also has medical uses.

Mechanism of action:- PAS has been shown to be a pro-drug and it is incorporated into the folate pathway by dihydropteroate synthase (DHPS) and dihydrofolate synthase (DHFS) to generate a hydroxyl dihydrofolate antimetabolite, which in turn inhibits DHFR enzymatic activity.

Uses

Tuberculosis

Aminosalicylic acid was introduced to clinical use in 1948. It was the second antibiotic found to be effective in the treatment of tuberculosis, after streptomycin. PAS formed part of the standard treatment for tuberculosis prior to the introduction of rifampicin and pyrazinamide. Its potency is less than that of the current five first-line drugs (isoniazid, rifampicin, ethambutol, pyrazinamide, and streptomycin) for treating tuberculosis.
and its cost is higher, but it is still useful in the treatment of multidrug-resistant tuberculosis. PAS is always used in combination with other anti-TB drugs.

The dose when treating tuberculosis is 150 mg/kg/day divided into two to four daily doses; the usual adult dose is therefore approximately 2 to 4 grams four times a day. It is sold in the US as "Paser" by Jacobus Pharmaceutical, which comes in the form of 4 g packets of delayed-release granules. The drug should be taken with acid food or drink (orange, apple or tomato juice). PAS was once available in a combination formula with isoniazid called Pasinah or Pycamisan 33.

The European Medicines Agency (EMA) has recommended granting a marketing authorization for PAS in multidrug-resistant tuberculosis in adults and children when other treatments cannot "be devised for reasons of resistance or tolerability."[7]

**Inflammatory bowel disease**

PAS has also been used in the treatment of inflammatory bowel disease (ulcerative colitis and Crohn's disease),[2] but has been superseded by other drugs such as sulfasalazine and mesalazine.

**Side effects**

- Gastrointestinal side-effects (nausea, vomiting and diarrhoea)
- It is also a cause of drug-induced hepatitis.
- With glucose-6-phosphate dehydrogenase deficiency should avoid taking aminosalicylic acid as it causes haemolysis.
- Thyroid goitre is also a side-effect because aminosalicylic acid inhibits the synthesis of thyroid hormones.
- Drug interactions include elevated phenytoin levels.
- When taken with rifampicin, the levels of rifampicin in the blood fall by about half.

**Kanamycin**

It is an aminoglycoside bactericidal antibiotic, available in oral, intravenous, and intramuscular forms, and used to treat a wide variety of infections. Kanamycin is isolated from the bacterium *Streptomyces kanamyceticus* and its most commonly used form is kanamycin sulfate. It is C_{18}H_{36}N_{4}O_{11} • 2H_{2}SO_{4}.D-Streptamine, O-3-amino-3-deoxy-α-D-
glucopyranosyl • (1→6)-O- [6-amino-6-deoxy-α-D-glucopyranosyl- (1→4)]-2-deoxy, sulfate 1:2 (salt). It consists of two amino sugars glycosidically linked to deoxystreptamine.

**Mechanism of action**

Kanamycin interacts with the 30S subunit of prokaryotic ribosomes. It induces substantial amounts of mistranslation and indirectly inhibits translocation during protein synthesis.

**Side effects**

- Nausea, vomiting.
- Loss of hearing.
- Toxicity to kidneys.
- Dizziness.
- Peripheral neuropathy, pain at the injection site and rashes.

**Drug interaction**

- Anesthesia drugs.
- Cisplatin.
- Diuretics.
- Muscle relaxers.
- Other antibiotics.

**A.D.M.E**

The drug is rapidly absorbed after intramuscular injection and peak serum levels are generally reached within approximately one hour. Doses of 7.5 mg/kg give mean peak levels of 22 mcg/mL. At 8 hours following a 7.5 mg/kg dose, mean serum levels are 3.2 mcg/mL. The serum half-life is 2 1/2 hours. Intravenous administration of Kanamycin over a period of one hour resulted in serum concentrations similar to those obtained by intramuscular administration.

Kanamycin diffuses rapidly into most body fluids including synovial and peritoneal fluids and bile. Significant levels of the drug appear in cord blood and amniotic fluid following intramuscular administration to pregnant patients. Spinal fluid concentrations in normal infants are approximately 10 to 20 percent of serum levels and may reach 50 percent when the meninges are inflamed.
Amikacin

Amikacin is an aminoglycoside antibiotic used to treat different types of bacterial infections. Amikacin works by binding to the bacterial 30S ribosomal subunit, causing misreading of mRNA and leaving the bacterium unable to synthesize proteins vital to its growth.

Uses

Amikacin is most often used for treating severe, hospital-acquired infections with multidrug-resistant Gram-negative bacteria such as *Pseudomonas aeruginosa*, *Acinetobacter*, and *Enterobacter*. *Serratia marcescens* and *Providencia stuartii* are also included in the spectrum. Amikacin can also be used to treat non-tubercular mycobacterial infections and tuberculosis (if caused by sensitive strains) when first-line drugs fail to control the infection. Amikacin may be combined with a beta-lactam antibiotic for empiric therapy for people with neutropenia and fever.

Liposomal amikacin for inhalation is currently in late stage clinical trials for the treatment of respiratory diseases, such as cystic fibrosis, *Pseudomonas aeruginosa*, non-tubercular mycobacterial infections and bronchiectasis.

Side effects

- Kidney damage.
- Hearing loss.
- Hypotension.
- Headache.
- Drug fever.
- Rash.
- Nausea.

A.D.M.E

Amikacin may be administered once or twice a day but must be given by the intravenous or intramuscular route or via nebulization. There is no oral form available as amikacin is not absorbed orally. In people with kidney failure, dosage must be adjusted according to the creatinine clearance, usually by reducing the dosing frequency.

Dose

General dose: -15 mg/kg/day divided IV/IM 8-12hr.
Urinary Tract Infection: 250 mg IV/IM q12hr.

Cipromycin: It is a Broad-spectrum antimicrobial drug of fluoroquinolone group with bactericidal action. Inhibits DNA gyrase and inhibits the synthesis of bacterial DNA. Highly active against most gram-negative bacteria: Pseudomonas aeruginosa, Haemophilus influenzae, Escherichia coli, Shigella spp., Salmonella spp., Neisseria meningitidis, Neisseria gonorrhoeae.

It is active against Staphylococcus spp. (including strains producing and not producing penicillinase, methicillin-resistant strains), some strains of Enterococcus spp., Campylobacter spp., Legionella spp., Mycoplasma spp., Chlamydia spp., Mycobacterium spp.

Cipromycin is active against bacteria producing beta-lactamases.

Mechanism of action

Cipromycin is a broad-spectrum antiinfective agent of the fluoroquinolone class. Cipromycin has in vitro activity against a wide range of gram-negative and gram-positive microorganisms. The mechanism of action of quinolones, including ciprofloxacin, is different from that of other antimicrobial agents such as beta-lactams, macrolides, tetracyclines, or aminoglycosides; therefore, organisms resistant to these drugs may be susceptible to ciprofloxacin. There is no known cross-resistance between Cipromycin and other classes of antimicrobials. Notably the drug has 100 times higher affinity for bacterial DNA gyrase than for mammalian.

Uses

It is an antibiotic that can treat a number of bacterial infections. It is a second-generation fluoroquinolone. Its spectrum of activity includes most strains of bacterial pathogens responsible for respiratory, urinary tract, gastrointestinal, and abdominal infections, including Gram-negative (Escherichia coli, Haemophilus influenzae, Klebsiella pneumoniae, Legionella pneumophila, Moraxella catarrhalis, Proteus mirabilis, and Pseudomonas aeruginosa), and Gram-positive (methicillin-sensitive, but not methicillin-resistant Staphylococcus aureus, Streptococcus pneumoniae, Staphylococcus epidermidis, Enterococcus faecalis, and Streptococcus pyogenes) bacterial pathogens. Ciprofloxacin and other fluoroquinolones are valued for this broad spectrum of activity, excellent tissue penetration, and for their availability in both oral and intravenous formulations.
It is used alone or in combination with other antibacterial drugs in the empiric treatment of infections for which the bacterial pathogen has not been identified, including urinary tract infections and abdominal infections among others. It can also treat infections caused by specific pathogens known to be sensitive.

**Side effects**
- Nausea, vomiting.
- Diarrhea, rashes.
- Abnormal liver function tests.

**Capreomycin**
Capreomycin is a peptide antibiotic, commonly grouped with the aminoglycosides, which is given in combination with other antibiotics for MDR-tuberculosis. Adverse effects include nephrotoxicity and 8th cranial auditory vestibular nerve toxicity. The drug should not be given with streptomycin or other drugs that may damage the auditory vestibular nerve. Patients on this drug will often require audiology tests.

**Mechanism of action**
It inhibits protein synthesis by binding to the 70S ribosomal unit. Capreomycin also binds to components in the bacterial cell which result in the production of abnormal proteins. These proteins are necessary for the bacteria’s survival. Therefore the production of these abnormal proteins is ultimately fatal to the bacteria.

**Side effects**
Serious side effects
- urinating less than usual or not at all;
- changes in your hearing;
- spinning sensation, problems with balance;
- ringing or roaring sound in your ears; or
- low potassium (confusion, uneven heart rate, extreme thirst, increased urination, leg discomfort, muscle weakness or limp feeling).

Less serious side effects may include
- mild skin rash;
- fever, chills, body aches, flu symptoms; or
- pain, swelling, or a hard lump where the injection was given.
Ethionamide
Ethionamide (INN; chemical name 2-ethylpyridine-4-carbothioamide) is an antibiotic used in the treatment of tuberculosis. It was discovered in 1956. It is sold under the brand name Trecator or Trecator SC by Wyeth Pharmaceuticals which was purchased by Pfizer in 2009. Ethionamide is part of a group of drugs used in the treatment of drug resistant TB called thioamides. It is used as part of treatment regimens, generally involving 5 medicines, to treat MDR and XDR TB. Ethionamide is used as part of a South Africa’s standard regimen to treat MDR TB. It has been proposed for use in combination with gatifloxacin.

Mechanism of action
Ethionamide is a prodrug. It is activated by the enzyme EthA, a mono-oxygenase in Mycobacterium tuberculosis, and binds NAD+ to form an adduct which inhibits InhA in the same way as isoniazid. Expression of the ethA gene is controlled by EthR, a transcriptional repressor. It is understood that improving ethA expression will increase the efficacy of ethionamide and so EthR inhibitors are of great interest to co-drug developers. The action may be through disruption of mycolic acid.

Side effects
- Diarrhea.
- Dizziness.
- Drowsiness.
- Headache.
- Increased salivation.
- Loss of appetite.
- Metallic taste, mouth sores, nausea.

Uses
Ethionamide is used with other medications to treat tuberculosis (TB). Ethionamide is an antibiotic and works by stopping the growth of bacteria. This antibiotic treats only bacterial infections. It will not work for viral infections.

REFERENCES


15. The journal of antibiotics 655,659 published online 6 august 2014.