|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **ISONIAZID (INH)**  **FIRST LINE AGENTS (ESSENTIALS) IN TREATMENT OF TB** | **RIFAMPIN / RIFAMPICIN** | **ETHAMBUTOL** | **PYRAZINAMIDE** | **STREPTOMYCIN** |
| Antimycobacterial activity | -bacteriostatic  -bactericidal  -penetrates cells so has similar concen. in and out cells | -potent bactericidal (wide range activity)  -kill intracellular and semidormant bacteria | -less active  -can kill M. Tuberculosis only  -suppress growth of most INH and strep. resistant TB | -**bactericidal** to **PERSISTERS** within cells | -kill extracellular TB |
| Mechanism of action | Inhibit synthesis of mycolic acids | Inhibit RNA synthesis | Inhibit synthesis of arabinoglycan | Inhibit enzyme that vital in FA synthesis | - |
| Enzyme activator | Mycobacterial catalase-peroxidase | - | - | Pyrazinamidase enzyme | - |
| Pharmacokinetics | -readily absorbed from GIT (oral)  -enzyme-inhibitor  -can cross BBB, so can treat TB meninges | -orally taken  -enzyme-inducer  -long half life  -give orange-red colour to urine, faeces, saliva, tears | -readily absorbed from GIT (oral)  -50% excreted by urine in unchanged form | -**resistance is not easy to acquire**  -action most active at **pH 5.5**  -readily absorbed from GIT (oral)  -metabolized in liver | -IV administration |
| Adverse effects | CNS  -peripheral neuropathy with numbness and tingling of the feet  -incoordination  -optic neuritis  -convulsions  LIVER  -inhibit metabolism of phenytoin causing excessive sedation  -liver injury  OTHERS  -hypersensitivity reactions  -SLE  -haemolysis in pt with glc-6-p dehydrogenase (deficient) | ALLERGIC  -influenza-like syndrome dt intermittent schedule  -thrombocytopenia  -cutaneous reactions  -pseudomembranous colitis  LIVER  -hepatitis  OTHERS  -nausea  -vomiting  -diarrhoea | MAIN  -optic neuritis  -red green colour blindness  OTHERS  -elevation of plasma uric acid  -drug fever  -rash  -joint pain  -GIT upset  -malaise  -numbness  -tingling | -arthralgia  Daily dosing>intermittent  -raised plasma uric acid concentration  -hyperuricemia  LIVER  -hepatitis  OTHERS  -anorexia  -nausea  -vomiting  -fever | -highly toxic but can be reduced by limiting therapy to NO more than 6 months |
| Clinical uses | -Treatment of TB  -As prophylaxis in single drug depends on few conditions. | -Treatment of TB  -Kill intracellular bacilli  -Chemoprophylaxisof meningococcal disease  + sulphones-leprosy  +vancomycin-treatment of serious staphylococcus infections | -Treatment of TB (bacteriostatic) in recommended dose.  CAUTION  Not for children <13, can cause visual impairment | -Acts as a “**sterilizing” agent which is active against residual intracellular organisms** which may cause relapse. **(decrease relapse rate)**  **-shorten duration of therapy to six months** | -Treatment of severe TB  -Treatment of infections resistance to other drugs  -enters CSF especially patient with inflamed meninges.  - might be used for short-course multiple drug therapy of TB |

Shunichi 10