

TB Medications:

What Nurses Need to Know

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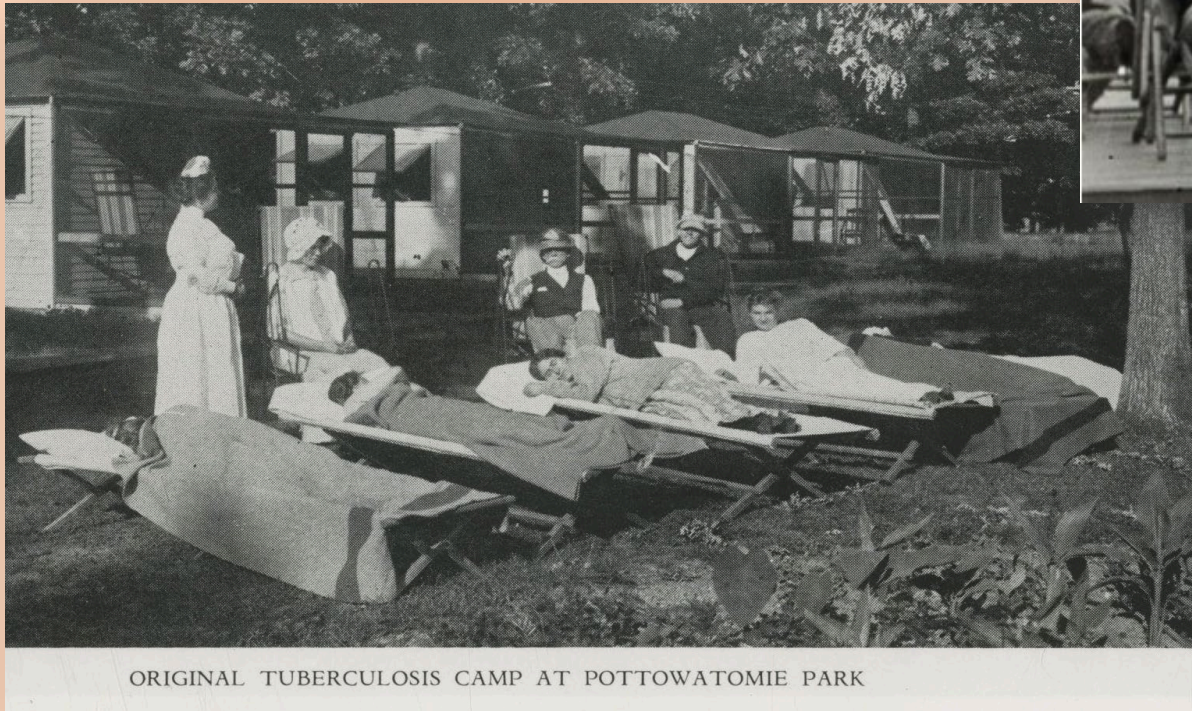


Objectives:

First-line Tuberculosis (TB) Medications

- Medication Dosages
- Side Effects
- Nursing Considerations
- Medication Administration Tips

TB Treatment before anti-tuberculosis drugs



Sanitoriums provided:

- ✓ Fresh air
- ✓ Sunlight
- ✓ Relaxing surroundings
- ✓ Good nourishment

Rifamycins



Rifampin
Rifabutin
Rifapentine

Isoniazid



Pyrazinamide



Ethambutol



Fluoroquinolones



Moxifloxacin
Levofloxacin

First-line Tuberculosis Drugs



Why use a Multi-Drug Therapy?



- *Mycobacterium tuberculosis* (MTB) produces resistant mutations during replication
- Multi-drug TB treatments provide cross-coverage against these various mutations
- Different actions of TB drugs
 - Bactericidal
 - Early Bactericidal
 - Bacteriostatic
 - Sterilizing

Actions of Anti-TB drugs:

Bactericidal

Directly kills the bacteria

**Early
Bactericidal**

Early reduction in colony forming units found in sputum; **isoniazid** has the highest EBA

Bacteriostatic

Prevents multiplication and growth

Sterilizing

Kill off "persisters"; **rifampin** has the highest sterilizing activity

RIFAMPIN

- **Bactericidal** (kills bacteria)
 - Highest sterilizing activity against rapidly dividing and semi-dormant bacteria
- **Dose:**
 - Adult: 10 mg/kg/dose (usually 600 mg PO)
 - Child: 15-20 mg/kg/dose
 - Infant/Toddler: 20-30 mg/kg/day
 - Renal failure/dialysis: no dose adjustment
- **Rapid absorption**
 - May be decreased by high-fat meals
 - CSF penetration
- **Increases metabolism of many drugs**
 - Hormonal contraception, methadone, anti-seizure medications, anti-coagulants, antiretrovirals



RIFAMPIN: Side Effects

Orange Discoloration



GI Upset



Pruritis



Hepatotoxicity



Less Common Side Effects

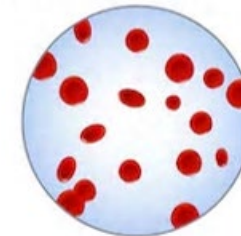
Flu-like symptoms

< 1% of
patients
Usually 3 – 6
months of
starting
treatment

Hyperbilirubinemia



Hemolytic Anemia



Thrombocytopenia



RIFAMPIN

- **Monitoring:**

- Liver enzymes AST/ALT if there are symptoms of hepatotoxicity
- Drug concentrations

- **Drug to drug interactions:**

- Certain rifamycins cannot be given with antiretroviral drugs; be sure to consult with an expert
- Ensure patient identifies all other medications they are taking as they may interfere with rifampin

- **Patient Education:**

- Best taken without food, however, can take with a small amount of food for stomach upset

RIFABUTIN



- Bactericidal (kills bacteria; same mechanism as rifampin)
- Dose:
 - Adult: 5 mg/kg/dose
 - Children: 5-10 mg/kg/day * (no pediatric dose has been established)
 - Renal failure/dialysis: no dose adjustment in mild renal insufficiency
 - Dosage adjustment may be required with anti-retroviral therapy
- Substitute for rifampin for patients receiving antiretrovirals
- Penetrates inflamed meninges
- Well absorbed from the GI tract
- Possible toxicity:
 - Leukopenia (decrease WBC's) thrombocytopenia (decrease PLT's) uveitis (redness, irritation, blurred vision, eye pressure)

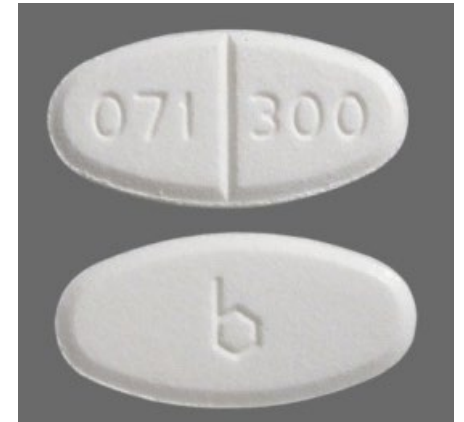
RIFAPENTINE



- Bactericidal activity (kills bacteria; same mechanism as rifampin)
- Approved for treatment of LTBI and more recently for TB disease in a new shorter course treatment regimen; dose varies on treatment regimen
- Adverse effects similar to rifampin

ISONIAZID

- **Bactericidal** (kills bacteria)
 - Accounts for majority of ***early bactericidal activity***; greatest early reduction in colony forming units found in sputum
 - Activated by ***katG*** enzyme
- **Dose:**
 - Adult: 5 mg/kg/day (300 mg/daily)
 - Child: 10-15 mg/kg/day
 - Renal failure/dialysis: 300 mg daily or 900 mg thrice weekly
- **Used for treatment of latent TB infection (LTBI) and active disease**



Isoniazid: Side Effects

Peripheral Neuropathy



Numbness or tingling of fingers and toes

CNS Changes



Restlessness and insomnia

Hepatotoxicity



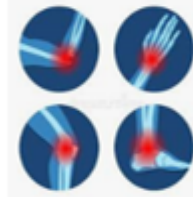
Increase in ALT/AST

GI Upset



Diarrhea, cramping, nausea, vomiting

Arthralgias/ Joint Pain



Baseline and monthly toxicity screening

Lupus-like syndrome

Flu-like symptoms <1%

Weakness, rash, muscle/joint pain, weight loss

Hypersensitivity Reactions



May present with fever or rash

ISONIAZID:

Patient Education and Monitoring

Patient Education:

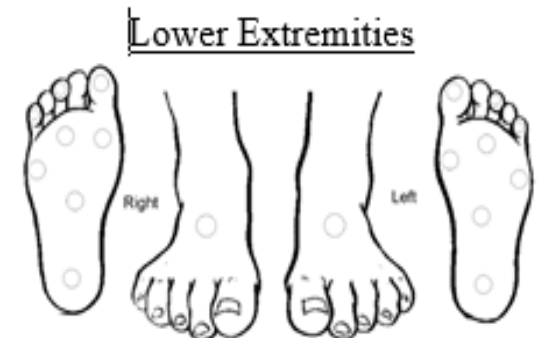
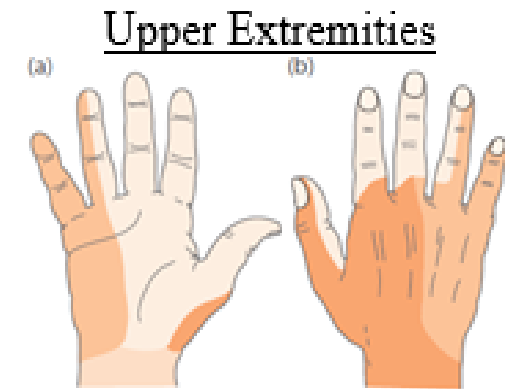
- Avoid alcohol
- Do not take antacids within one hour of medication administration
- Some patients may benefit from supplemental Vit B6
- Drug interactions:
 - levodopa, phenytoin, valproic acid, carbamazepine



Monitor:

- LFTs: baseline and monthly, especially if underlying liver disease exists
- Therapeutic drug monitoring is recommended if you suspect malabsorption or treatment failure

Urine		g/dL
To		/dL
Alt		
Glob		me
Total b		U/L
Direct bilirubin	220 H	U/L
AST (SGOT)	340 H	U/L
ALT (SGPT)		U/L
ALP		U/L



PYRAZINAMIDE

- **Bacteriostatic/sterilizing agent:**
 - Greatest activity against dormant or semi dormant (slow growing) organisms
- **Dose**
 - Adult: 25mg/kg/day
 - Children: 30-40 mg/kg/dose
 - Renal failure: 25 mg/kg/dose 3 times per week (not daily)
 - Cleared by the kidneys; *dose 3 x week after dialysis*
- **Use in pregnancy/breastfeeding:**
 - In the U.S. PZA is avoided in pregnancy for drug susceptible disease due to lack of data regarding teratogenicity, however
 - Should be used for drug-resistant TB when the isolate is susceptible to PZA
 - When in doubt, please consult with an expert



PYRAZINAMIDE

- **Adverse Reactions:**

- Gout (hyperuricemia) and arthralgias
- Hepatotoxicity
- Rash
- Photosensitivity
- GI upset

- **Monitor**

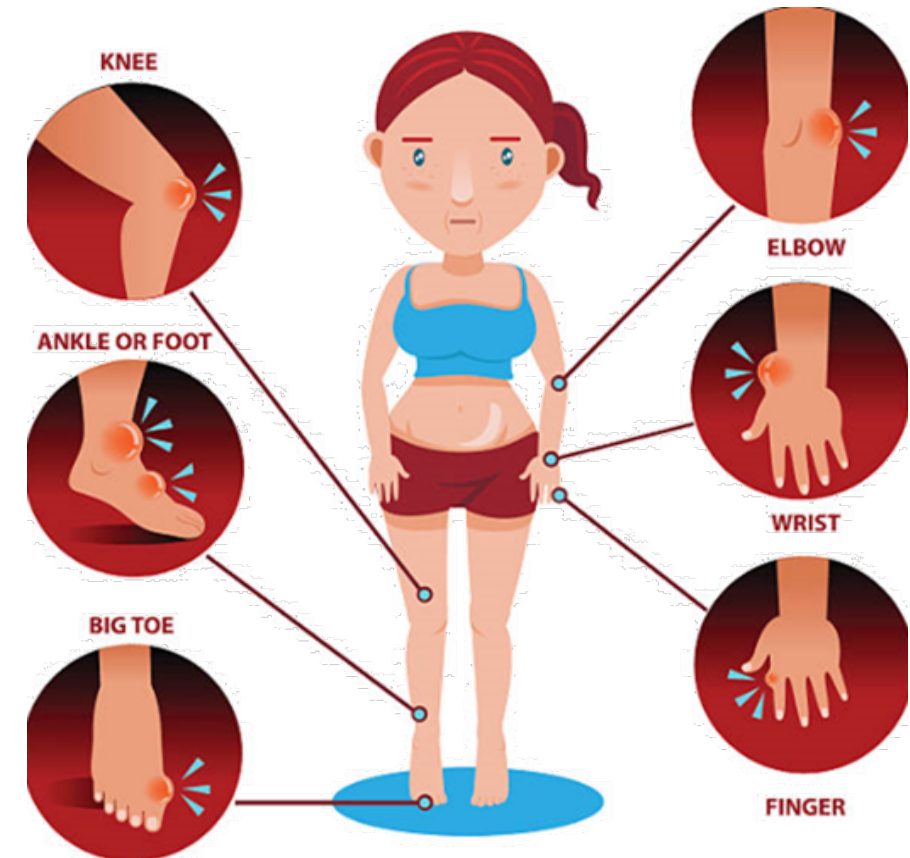
- Monitor transaminases and uric acid

- **Patient educations:**

- May be taken with or without food
- Limit sun exposure
- Notify nurse or healthcare worker if they experience severe pain or swelling in joints



BS/Glucose		mg
Cholesterol		mg/dL
Triglyceride		g/dL
HDL-C		g/dL
LDL-C	12.5 H	g/dL
Uric acid		g/dL
Total protein		g/dL
Albumin		mg/dL



ETHAMBUTOL

- **Bacteriostatic** (prevents multiplication/growth)
 - Bactericidal only at the high end of the dosing range
- **Prevention of rifampin resistance:**
 - Ethambutol **protects the emergence of rifampin resistance** when INH resistance may be present
- **Dose:**
 - Adults: 15-25 mg/kg/day
 - Children: 15-25 mg/kg/day
 - Renal failure: 15-25 mg/kg/dose 3 x weekly (not daily)
- Remember: EMB can be discontinued as soon as the results of drug susceptibility studies demonstrate that the isolate is susceptible to INH and RIF



ETHAMBUTOL

- **Toxicity**

- Retrobulbar neuritis
 - Can be in one or both eyes
- Peripheral neuritis
- Cutaneous reactions (<1%)

- **Monitor**

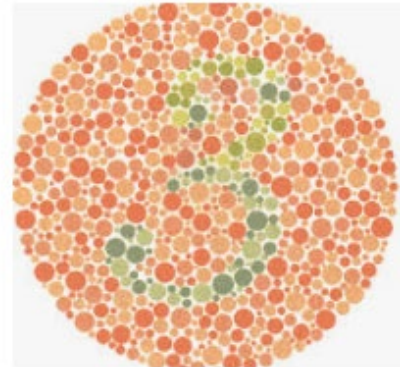
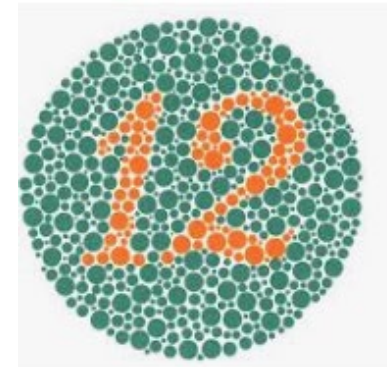
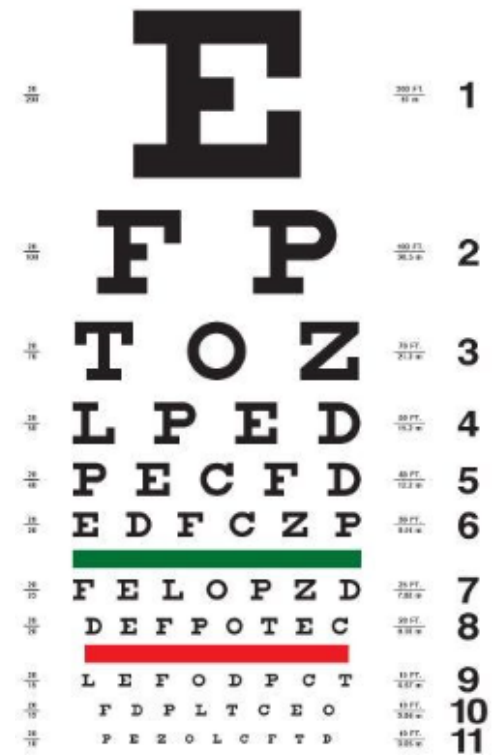
- Baseline and monthly visual acuity (Snellen) and color discrimination (Ishihara) should be performed
- Monitor blurry vision (squinting during exam or difficulty seeing traffic signs)



If changes from baseline occur, stop medication and refer to ophthalmologist

- **Patient Education:**

- Counsel patient to report any visual changes



FLUOROQUINOLONES

Moxifloxacin



Levofloxacin



FLUOROQUINOLONES

Moxifloxacin

Bactericidal

Metabolized in part by the liver

Dose: 400 mg/day; no dose adjustment required with renal insufficiency

Levofloxacin

Bactericidal

Excreted unchanged by the kidneys;

Dose: 750-1000 mg/day; adjust dose in renal insufficiency (750-1000 mg/dose 3 times weekly for creatinine clearance < 30 mL/min).

Side Effects	Abdominal discomfort	Diarrhea	Nausea/vomiting	Mouth sores	Headache	Dizziness
	Skin itching	QT prolongation	Blurred vision	Nervousness	Anxiety	Agitation

Fluoroquinolone Toxicity

- Hepatotoxicity (**rare** with levofloxacin)
 - Reversible transaminase elevation
- Tendonitis/Tendon Rupture; **rare**
 - Usually achilles
 - Risk benefit evaluation
- Neurologic effects
 - Insomnia, dizziness, headache, tremors
- ***Patient Education:***
 - Avoid milk-based products or antacids within 2-hours of ingesting medication
 - Avoid vitamin supplements

Medication Administration Tips for Adults

Crush meds
and place in
applesauce or
in a drink of
patient's
choice

Drink water
before taking
medications
to lubricate
throat

Try to take a
couple of pills
at a time
rather than
one by one



Medication Administration Tips for Children

- Crush medications and mix them into something sweet (contact pharmacy to ensure medication can be crushed)
- Role play medication administration with a stuffed animal
- Medications should be administered within 30 minutes of mixing



Don't forget to visit Heartland National TB Center: Products and Tools



[Products – Heartland National TB Center](http://heartlandntbc.org)
[\(heartlandntbc.org\)](http://heartlandntbc.org)

Tips for Treating Latent TB Infection in Children

Including Window
Prophylaxis

Who should be treated?

- ▶ **Children with latent tuberculosis (TB) infection (LTBI)** - where LTBI is defined as a positive TB screening test (tuberculin skin test [TST] or interferon gamma release assay [IGRA] blood test) and no evidence of active disease on chest x-ray (CXR) or physical exam.
- ▶ **Children in the window period after exposure** - Children <5 years old who have been in contact with an infectious adult or teen in the past 8 weeks and who have a negative TB screening test are still in the window period for test conversion. These children should have a physical exam and CXR. If there is no evidence of active disease, they should be treated with 'window prophylaxis' and retested 8-10 weeks after the break in contact with the infectious source.
- ▶ **Children who are in contact with a source that has drug resistance** - Whether the infectious source has multidrug-resistant (MDR) or other drug resistant TB, children who are exposed or infected should be treated in consultation with an expert in tuberculosis.



What are the treatment regimens?

- ▶ **3HP** - (isoniazid [INH] and rifapentine [RPT]) is approved for children ≥ 2 years of age. This regimen allows a child to be treated with only 12 weekly doses of medication.
- ▶ **4R** - (rifampin [RIF] daily for 4 months) is safe and effective for children that cannot take 3HP.
- ▶ **3HR** - (INH and RIF dosed daily for 3 months) though not used as commonly in the United States (US) as in the United Kingdom, is an effective short-course treatment regimen.
- ▶ **6H** - (INH dosed daily or twice weekly [BIW]) is effective, but the least desirable, as only 50% of patients are likely to complete the necessary 6 months course.
- ▶ Infants who are exclusively breastfed, pregnant teens and children with poor diets or who are immune suppressed should receive pyridoxine (Vitamin B6) 1-2 mg/kg with each dose of INH.

What are helpful administration tips?

- ▶ To help with swallowing pills, children can practice by swallowing similarly sized candies.
- ▶ For children who cannot swallow pills, TB medications can be crushed (or capsules opened) and mixed with a small amount of food (syrup, applesauce, etc.).
- ▶ Mixing should be done immediately before dosing and discarded if not administered within 30 minutes of mixing.



What are the monitoring recommendations?

- ▶ Medication doses should be adjusted based on weight change, if needed.
- ▶ Children tolerate treatment very well. Routine laboratory monitoring is not necessary unless the child takes other medications metabolized through the liver or has liver disease.
- ▶ Children taking other medications or who have underlying liver conditions should have a monthly CBC (complete blood count) as well as a metabolic panel that contains liver function tests (LFTs).
- ▶ Children with symptoms that suggest medication toxicity (e.g. recurrent vomiting, decreased appetite, abdominal pain) should have their LFTs checked.

- All TB medications have side effects
- Baseline and monthly assessments for visual acuity and color discrimination aid in preventing toxicities
- When changes from baseline occur
 - Hold medications and reassess the patient to find likely cause
- Be creative when medication administration becomes a challenge



**Take
home message*

Thank You!