

# Management of Medication Side Effects and Toxicities During Treatment for NTM Infections

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**THE MEDICATIONS ARE WORSE  
THAN THE DISEASE**



# Rifampin/Rifabutin



Usual dose is 300mg ( 2 pills)

Usual dose is 600mg (2 – 300mg pills)

If >110 pounds. Decrease dose to 45mg

If < 110 pounds.

- I suggest taking both pills at the same time on an empty stomach.
- I suggest taking this medication at bedtime with 1 saltine cracker and just a couple sips of water.

# Toxicity - Nausea and vomiting



# Any Drug Can Cause a Rash



# Rifampin/Rifabutin

- Rash
- Fever, Joint aches, “Feels like I have the flu”
- Nausea and vomiting
- Blood test abnormalities
  - Elevated liver tests
  - Low white blood cell numbers
  - Low platelets
- Have CBC and Biochem panel done at least once a month

# Ethambutol



# Ethambutol

- Usually you will take 2 or 3 (sometimes 4) of these pills
- Take the full dose at one time
- **DON'T TAKE 1 WITH BREAKFAST, LUNCH AND DINNER!**
- These are best taken on an empty stomach and I usually suggest taking them 1 hour before breakfast (usually with azithromycin)

# Ethambutol – Side Effects

- Optic Neuritis
  - Read small print daily
  - If blurry vision occurs 2 days in a row, **STOP THE ETHAMBUTOL IMMEDIATELY** and go see your ophthalmologist as soon as possible
  - Blurry vision can also occur with cataracts, but don't just assume the vision changes are due to cataracts



# Ethambutol – Side Effects

- Rash
- Nausea is rare
- Liver test elevation
- Have CBC and Biochem panel done monthly



# Azithromycin



- Gastrointestinal side effects are most common
  - Eliminate more frequently
  - May have loose stools
- Tinnitus and Hearing loss
  - Have your hearing checked at least every 6 months or much more frequently if you already have baseline hearing loss
  - Many of us are genetically predisposed to hearing loss and azithromycin may add to your chances of developing it



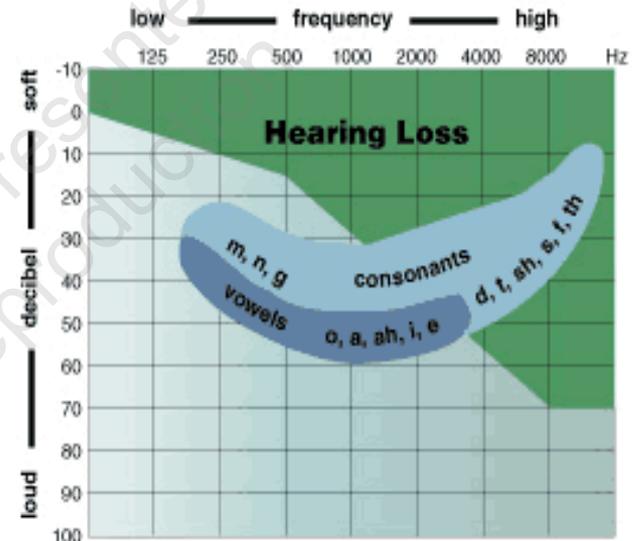
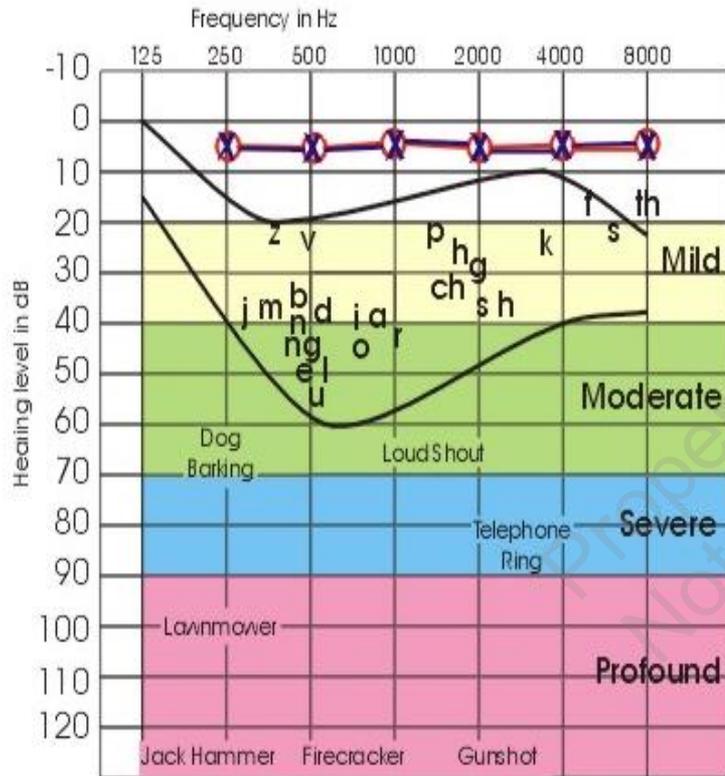
# Clarithromycin



- Gastrointestinal side effects are most common and generally more pronounced than with azithromycin
  - Metallic taste
  - Diarrhea
  - Intestinal cramping
- Tinnitus and hearing loss just as with clarithromycin

# Hearing Loss Monitoring

AUDIOGRAM



Hearing Range (with common hearing loss)

# Tricks of the Trade to Manage Side Effects

- Take probiotics
  - Mixed data regarding their use, but I am a big proponent
- Take ethambutol and azithromycin/clarithromycin 1 hour before breakfast and rifampin/rifabutin at bedtime. Take the rifampin with 1 saltine cracker and just a few sips of water
- Monitor your vision DAILY by reading small print. Do it the same way each day

# Tricks of the Trade to Manage Side Effects

- Report ANY side effects to your physician
- If you are having vision changes
  - STOP THE ETHAMBUTOL IMMEDIATELY
  - MAKE AN APPOINTMENT TO SEE YOUR EYE DOCTOR
  - TELL YOUR PHYSICIAN WHAT IS GOING ON
  - DO NOT CONTINUE THE ETHAMBUTOL UNLESS YOU HAVE BEEN CLEARED BY THE OPTHOMOLOGIST

# Amikacin

- May be given as an intravenous medication 3 times a week through a PICC line
- Usually given for between 2 and 6 months
- Side effects of a PICC line MAY BE
  - Blood clot in the arm
  - Bloodstream infection
- **DO NOT LET ANYONE DRAW BLOOD FROM THE PICC LINE! IT IS ONLY TO BE USED TO ADMINISTER MEDICATION**

# Amikacin

- **Hearing** must be monitored closely
- **Kidney tests** must be monitored closely

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# Amikacin

- Get an audiogram AT LEAST every month while on intravenous amikacin. YOU MAY NEED IT EVERY ONE TO TWO WEEKS IF YOU ALREADY HAVE SIGNIFICANT HEARING LOSS
- An audiogram DOES NOT help with following tinnitus (also ear fullness, whooshing sounds, etc). You need to stop the IV amikacin immediately if you experience any of these symptoms lasting more than 1 minute and don't take any more doses until you have discussed these issues with your physician



# Inhaled Amikacin

ARIKAYCE

- Two current formulations
  - Liposomal amikacin nebulized formulation.
    - 590mg nebulized once daily with eFlow nebulizer
  - Intravenous form of the amikacin that is diluted with saline and then placed in a nebulizer cup and nebulized anywhere from three times a week to 7 days a week
- Even if given nebulized, you will need to have hearing testing done periodically and blood testing for kidney functioning periodically. We don't know exactly how frequently monitoring is necessary

# Amikacin

- You must use the filter on the nebulizer if you are using the nebulizer in common space with humans and animals. They can absorb these medicines with prolonged exposure





# Clofazimine



- New, old drug
- Currently only available in the USA through application with the FDA
- Your physician has to fill out the application, the application (IND) must be presented to an IRB (Institutional Review Board). If approved, you will get the medication for free





# Clofazimine



- Starting dose is 100mg once daily however if side effects develop, decreasing the dose to 50mg once daily or even 50mg three times a week will often help
- Most common side effect is gradual skin tanning. This skin discoloration will begin to fade away once the medication is discontinued
- Some patients complain of stomach upset or intestinal cramping although this is not common
- A baseline EKG and periodic repeat testing should be done while on this medication

# Imipenem

- An intravenous medication that must be administered with a PICC line
- Given for the Rapidly Growing Mycobacteria such as *M. abscessus* but also for other “Respiratory Bacteria” such as *Pseudomonas*
- Usually administered twice a day
- Side effects are rash, diarrhea (*C. diff*), and rarely liver inflammation

# Imipenem

- Rarely, patients will have an “allergic” reaction that is best described by patients as “I just want to die”. They may have fever, body aches, terrible fatigue
- These symptoms will resolve within a day or two once the medication is stopped
- You should have blood monitoring with CBC and Biochem panel every week or two while on this antibiotic

# Cefoxitin

- This is an intravenous antibiotic used to treat the Rapidly Growing Mycobacteria such as M. abscessus
- It has a much higher risk of rash (it is a close cousin of penicillin) than imipenem, so we don't use it as often
- Common side effects are rash and C. difficile diarrhea
- You should have a CBC and Biochem panel done every week or two while on this medication

# Tigecycline

- An intravenous medication that is used if your germ is resistant to other medications used to treat Rapidly Growing Mycobacteria such as M. abscessus
- This medication has significant associated nausea, vomiting and may cause many disturbances in liver tests and electrolytes.
- It is best to pre-medicate with anti-nausea medications at least 30 minutes prior to the dose. It is given once or twice a day. Slowing the infusion rate WILL NOT HELP.



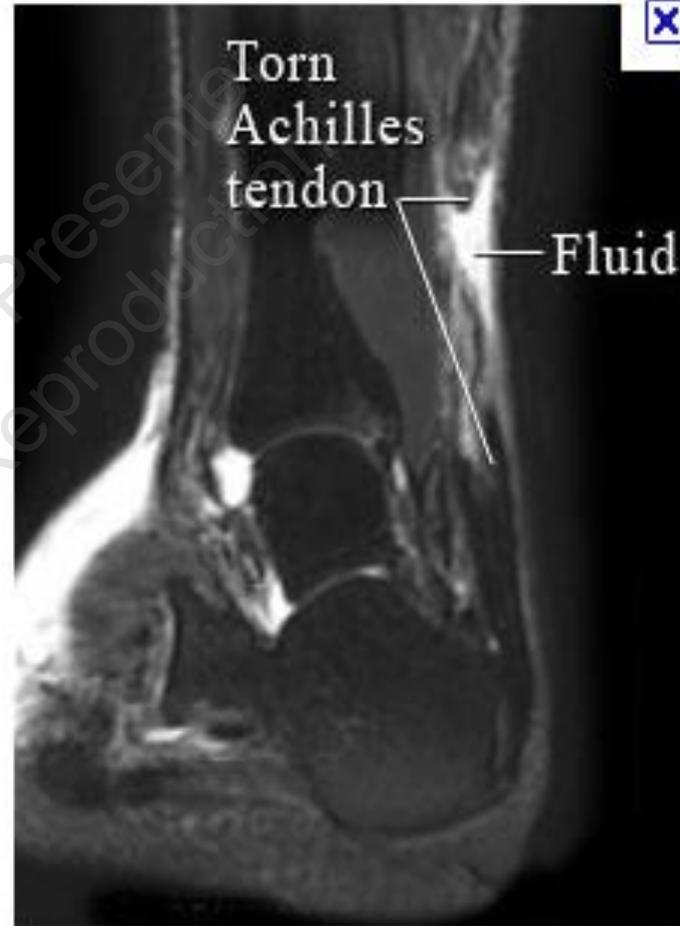
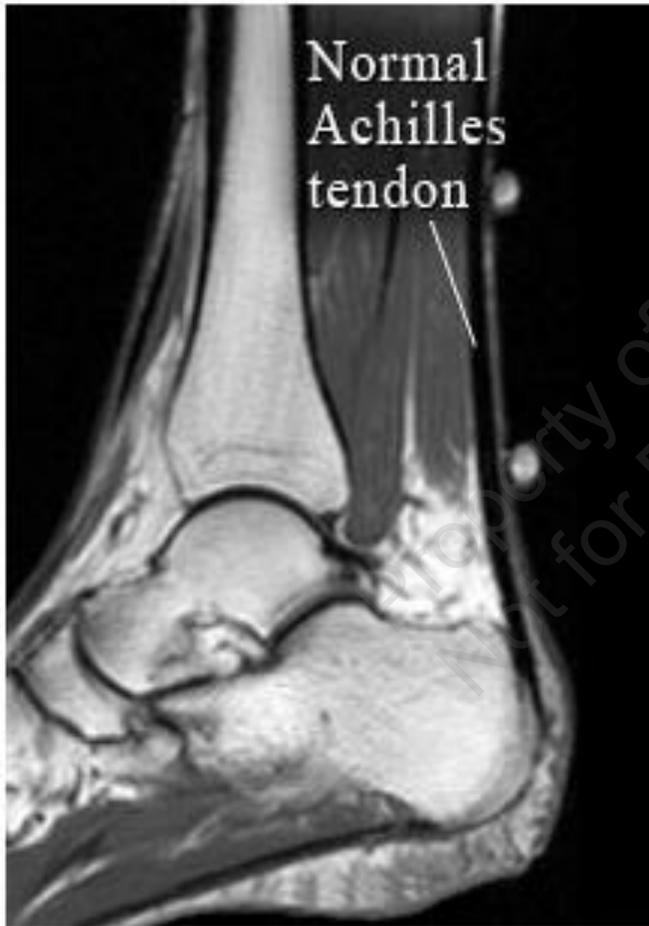
# Linezolid

- This is an oral medication that is given primarily for the treatment of MRSA infections but is also useful at times to treat Rapidly Growing Mycobacteria organisms
- It is generally fairly well tolerated for the first few days to weeks, but has a high incidence of causing inflammation of peripheral nerves of the fingers and toes (neuritis) and also can cause suppression of the bone marrow.

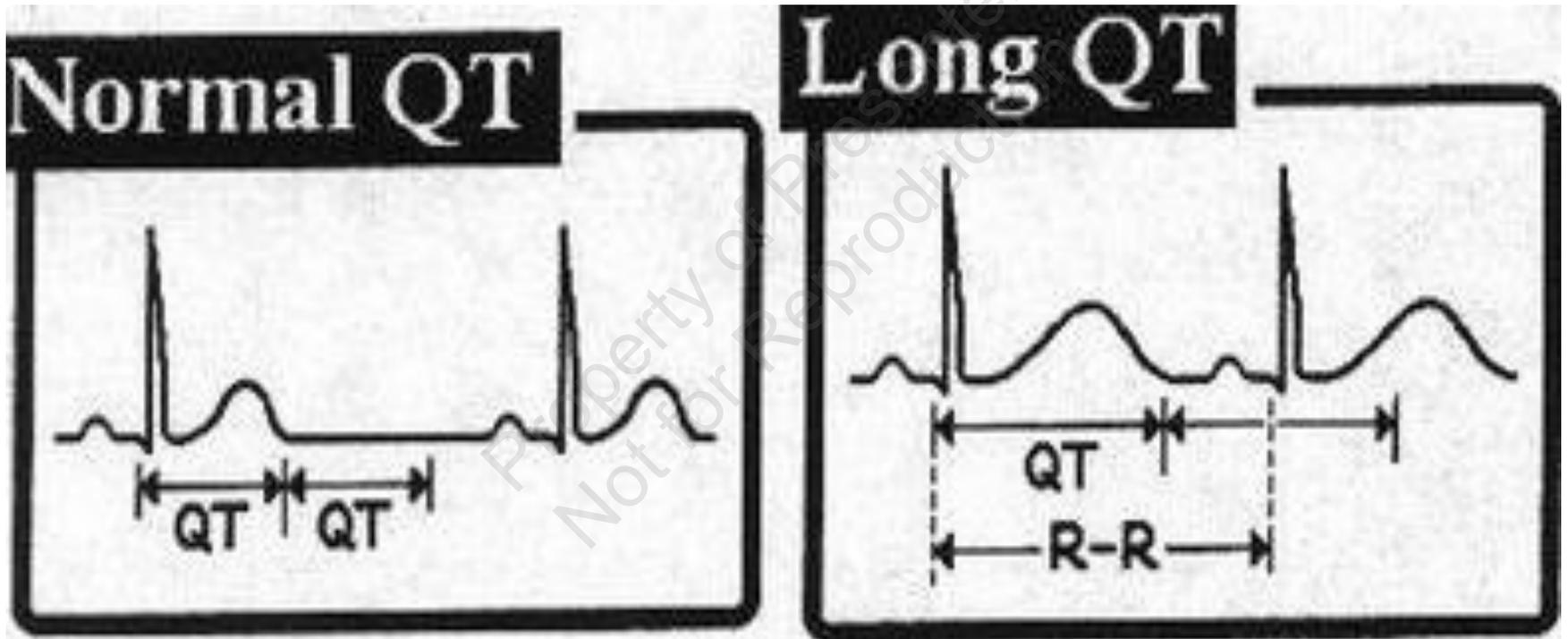
# Levofloxacin/Moxifloxacin

- Not usually active against most types of mycobacteria
- It is however, pretty active against many mouth and stomach germs
- Inflammation of the tendons can be a real problem (think ruptured Achilles tendon). If you experience “joint pain” while taking these medications, it is probably a sign of tendon inflammation and the antibiotic should be stopped!
- Can also cause abnormalities in the heart electrical system
- These medications have a caffeine effect and can interfere with sleep.
- Don't take within 2 hours of dairy, antacids or vitamins or calcium supplements

# Ruptured Achilles Tendon



Prolonged QT with levo/moxifloxacin,  
azi/clarithromycin, and clofazimine



# Bottom Line

- The treatment should not be worse than the disease
- Keep a treatment journal
  - What time do you take each medication
  - What time did you have a reaction
  - What was the reaction
  - What made it better or worse
- Communicate closely with your physician!

# Thank You!



# Questions?