

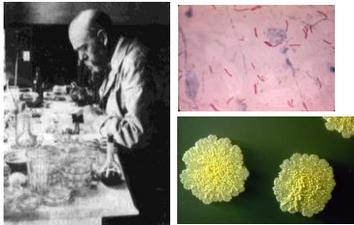
Tuberculosis Diagnosis and Treatment

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Tuberculosis

- ▶ May have evolved from *M. bovis*
 - Acquired by humans from domesticated animals about 8,000 BC
 - Became endemic in humans when stable networks of 200–440 people established (villages) about 8000 BC
- ▶ Epidemic in European cities after 1600
- ▶ Possibly introduced into sub-Saharan Africa, East Asia and Pacific Islands from Europe

M. tuberculosis as Causative Agent for TB



In 1882, Robert Koch presented his discovery of the TB causing bacterium in 1882 (Koch also discovered anthrax and cholera bacteria.)

The Mycobacteria

- ▶ Mycobacteria
 - Numerous occurring zoonotically and in environment
 - Named species increases daily!
 - Most not a human or public health concern
 - Non-tuberculous mycobacteria (NTM)
- ▶ Human pathogens
 - *M. tuberculosis* Complex
 - *M. tuberculosis*, *M. bovis*, *M. microti*, *M. canetti*, *M. africanum*
 - New members – *M. caprae*, *M. pinnipedii*, *M. mungi*
 - Most cause disease in humans
 - Respond as active TB if ill
 - *M. leprae*

Transmission of TB

- ▶ TB spreads from person to person through the air

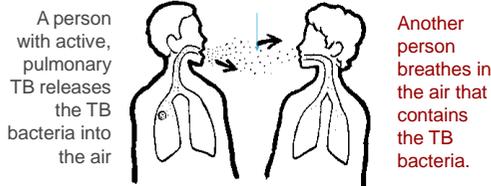


Transmission of TB

- ▶ Airborne by droplet nuclei – 1–5 microns in diameter
- ▶ Can remain suspended for several hours
- ▶ Not transmitted by surface contact

TB: Airborne Transmission

TB bacteria becomes airborne



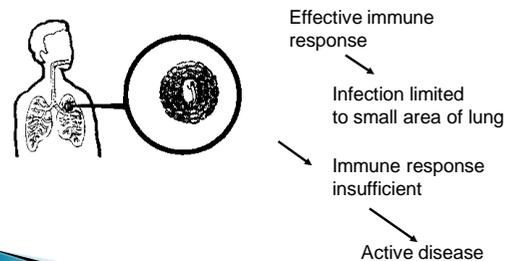
Probability of TB Transmission

- ▶ Transmission depends on the following factors
 - Infectiousness of the person with TB
 - Environment in which the transmission occurs
 - Duration of the exposure to TB bacteria
 - Susceptibility of the exposed individual

Pathogenesis of TB

- ▶ Infection begins when the inhaled droplets reach the lungs
- ▶ Tubercle bacilli multiply
- ▶ A small number of tubercle bacilli may enter the bloodstream and spread throughout the body (lungs, kidneys, brain, bone)
- ▶ Within 2-10 weeks, the immune system produces a capsule that surround the tubercle bacilli

TB Invades/Infects the Lung



Latent TB Infection vs. Active TB Disease

Latent TB Infection (LTBI)	Active TB Disease
Tubercle bacilli in the body	
Tuberculin skin test reaction usually positive	
Chest x-ray usually normal	Chest x-ray usually abnormal
Sputum smears and cultures negative	Sputum smears and cultures may be positive
No symptoms	Symptoms such as cough, fever, weight loss
Not infectious	Often infectious before treatment
Not a case of TB	A case of TB

Sites of TB Disease

- ▶ Pulmonary TB (TB of the lungs)
 - 85% of cases
 - Potential for transmission - infectious until proven otherwise
- ▶ Extrapulmonary TB (outside the lungs)
 - Can occur anywhere in body
 - Portal of entry through lungs
 - Typical sites include larynx, lymph nodes, the pleura, brain, kidneys, bones, or joints
 - Usually not infectious - always rule out pulmonary!
- ▶ Respiratory sites of disease

Likelihood of Developing TB Disease

- ▶ Once infected with tubercle bacilli
 - 90% chance of never developing the disease
 - 10% life time chance that TB disease will develop
 - Half the risk within the first 2 years
 - Risk lower after the first 2 years
 - Other personal health factors can influence risk
 - HIV infection – single highest risk for progress to active disease
 - 10% annual risk

Relative Risk of Developing Active TB Disease

Risk Factor	Risk Increase
AIDS	170 times
HIV infection	113 times
Recent infection	15 times
Certain Medical Conditions	3-16 times

TB Diagnosis

- ▶ “The first rule of TB diagnosis: is to think TB....”

Diagnosis of Pulmonary TB

(80–85% of TB Cases)

- ▶ Chest x-ray
 - Standard PA and lateral films; apical lordotic views may be helpful
 - Infiltrates, nodular densities, cavities, +/- hilar adenopathy
 - Abnormalities may be subtle or non-existent in immuno-compromised patients
 - Previous x-rays for comparison may be useful
- ▶ CT scans
 - Often obtained
 - Nice to have but rarely critical to diagnosis
 - Expensive

Diagnosis of Pulmonary TB

- ▶ Laboratory tests
 - A continuum of testing
 - AFB smear – 24 hours
 - NAA – MTD – few days after smear
 - Culture – preliminary 7–14 days
 - Positive for an Nontuberculous mycobacteria does not rule out TB
 - ID of isolate – confirmation of *M.tb* or not
 - Antimicrobial susceptibility testing – 28 days

Diagnosis of Pulmonary TB

- ▶ TST and IGRAs
 - Positive supports but does not make diagnosis
 - Negative does not exclude TB as possible diagnosis

Diagnosis of Pulmonary TB

- ▶ Coughed sputum
 - Best specimen when available
 - Early AM best, supervise at least one collection
 - AFB smear best available tool for assessing infectiousness
 - Most likely to yield positive culture
 - Multiple specimens recommended to maximize chances for +AFB/culture

Yield of smear and culture from repeated sputum induction for the diagnosis of pulmonary tuberculosis

	Induced sputum (% yield)			
specimen	one	two	three	four
AFB smear	64	81	91	98
AFB culture	70	91	99	100

Int J Tuberc Lung Dis. 2001 Sep;5(9):855-60. Al Zahrani K, et al.

Laboratory Tests for *M.tb*

- ▶ AFB smear
 - Available in 24–48 hours
 - Simple test; requires skilled technologist to read
 - Not diagnostic for *M.tb*: All AFB look alike
 - Used to assess infectiousness
 - Need for isolation, contact investigation
 - Monitor response to treatment
 - Decrease in AFB on smear correlates with effectiveness of treatment

Laboratory Tests for *M.tb*

- ▶ Culture and Identification of Isolate
 - “Gold standard” for TB diagnosis
 - Usually complete in 2–4 weeks
 - Not signed out as negative until 8 weeks
 - Traditional identification based on growth characteristics, biochemical tests
 - Preliminary ID by “probe” now standard
 - Requires isolate (2–4 weeks)
 - Tests DNA – can ID *M.tb complex*, *M.avium*, +/- others
 - More rapid than chemicals, just as accurate
 - Cannot distinguish among *M.tb complex* species (*M.tb* vs. *M.bovis*)

Laboratory Tests for *M.tb*

- ▶ Antimicrobial susceptibility testing
 - Requires isolate
 - 2–4 weeks after isolate available
 - IREZ +/- S testing standard
 - Second line drug testing only on request
 - 3–10% of VA TB isolates resistant to ≥ 1 first line TB drug
 - Continue IREZ until susceptibility results available

Direct/rapid tests for TB

- Nucleic acid amplification – DCLS using MTD
- Results in 3–5 days
- Automatically done for positive smears
- TB Control must request on negative smears
- Cannot be on treatment for more than 7 days or within last 12 months
- Beware “the probe”

Other Diagnostic Tests

- ▶ HAIN Test – rapid molecular susceptibility testing for INH and rifampin
 - Requires authorization
 - Can be done from raw specimen
- ▶ CDC molecular susceptibilities
 - Requires authorization
 - Requires growing culture – i.e. preliminary culture report

Treatment of Tuberculosis

Treatment of TB Disease

- ▶ Overall goals
 - Cure the individual patient
 - Minimize transmission within the community
- ▶ Responsibility for successful treatment is assigned to public health department or private provider, not individual patient.
- ▶ Health department **ultimately responsible** for ensuring adequate, appropriate treatment.

Treatment of TB Disease

- ▶ 4 regimens approved for drug susceptible disease
- ▶ Recommendations for HIV–infected same with a few exceptions
 - Twice weekly options are not recommended for HIV+ patients with CD4+ cell counts less than 100

Antituberculosis Drugs Currently in Use in the United States

- ▶ First–line Drugs
 - Isoniazid
 - Rifampin
 - Rifapentine
 - Rifabutin*
 - Ethambutol
 - Pyrazinamide
- ▶ Second–line Drugs
 - Cycloserine
 - Ethionamide
 - Levofloxacin*
 - Moxifloxacin*
 - Gatifloxacin*
 - *P*-Aminosalicylic acid
 - Streptomycin
 - Amikacin/kanamycin*
 - Capreomycin

Treatment Pearls

- ▶ Ethambutol can be discontinued once susceptibility to INH and RIF demonstrated
 - Must be on PZA
 - Requires physician order
- ▶ PZA must be continued for full recommended 8 week course to qualify for short–course treatment
 - Number of doses depends on prescribed regimen
 - Dose count required
- ▶ DOT standard of care for all
- ▶ Never add a single drug to a failing regimen

Drug Regimens for Culture-Positive TB with Drug Susceptible Organisms

Regimen 1

- Initial phase
 - INH/RIF/PZA/EMB
 - 7 d/wk for 56 doses (8 weeks)
 - Option – 5 d/wk for 40 doses (8weeks)
- Continuation phase
 - INH/RIF
 - 7 d/wk for 126 doses (18 weeks)
 - 5 d/wk for 90 doses (18 weeks)
 - Twice weekly for 36 doses (18 weeks)*
 - INH/RPT
 - Once weekly for 18 doses (18 weeks)*

Drug Regimens for Culture-Positive TB with Drug Susceptible Organisms

Regimen 2

- Initial phase
 - INH/RIF/PZA/EMB
 - 7 d/wk for 14 doses (2 weeks)
 - Then twice weekly for 12 doses (6 weeks) *
 - OR
 - 5 d/wk for 10 doses (2 weeks)
 - Then twice weekly for 12 doses (6 weeks)*
- Continuation phase
 - INH/RIF
 - Twice weekly for 36 doses (18 weeks)*
 - INH/RPT
 - Weekly for 18 doses*

Drug Regimens for Culture-Positive TB with Drug Susceptible Organisms

Regimen 3

- Initial phase
 - INH/RIF/PZA/EMB
 - Three times weekly for 24 doses (8 weeks)
- Continuation phase
 - INH/RIF
 - Three times weekly for 54 doses (18 weeks)

Drug Regimens for Culture-Positive TB with Drug Susceptible Organisms

Regimen 4

- Initial phase
 - INH/RIF/EMB
 - 7 d/wk for 56 doses (8 weeks)
 - or
 - 5 d/wk for 40 doses (8 weeks)
- Continuation phase
 - INH/RIF
 - 7 d/wk for 217 doses (31 weeks)
 - 5 d/wk for 155 doses (31 weeks)
 - Twice weekly for 62 doses (31 weeks)*

Completion of Treatment

- ▶ Determination made more accurately by total number of doses taken, not time period
- ▶ Goal is to deliver the recommended specified number of doses in a maximum time frame
 - Important in cases of non-adherence, toxicity
 - 6 month regimen should be completed in 9 months
 - 9 month regimen should be completed in 12 months
- ▶ Non-standard treatment due to drug resistance or intolerance – longer, more complicated
 - Depends on missing drug or drugs

Management of Initial Phase Treatment Interruptions

- ▶ Management of lapses dependent on
 - Phase of treatment when lapse occurs
 - First 8 weeks – need for restart likely if prolonged
 - Duration of the lapse in treatment
 - Results of patient evaluation when treatment restarted
- ▶ Contact TB Control for assistance

TB Medications



Isoniazid



- Preparation
 - 50 mg, 100 mg, and 300 mg tablets
 - Suspension (can cause diarrhea and cramping)
 - Only commercially prepared suspension
 - Must be kept at room temperature
- Administration tips
 - Can be cut or crushed
 - Mix with food just before administering
 - Do not take with large fatty meal
 - If upsets stomach, take with small amount of food
 - Avoid alcohol or OTC meds such as Tylenol or other pain relievers
 - No antacids within 1 hour

Isoniazid



- Adverse Reactions and Side effects
 - Hepatitis
 - Loss of appetite
 - Tiredness, weakness
 - Stomach pain, nausea, vomiting
 - Yellow skin or dark colored urine
 - Can cause flushing with some fish or cheeses
 - Peripheral neuritis
 - Numbness or tingling in hands or feet
 - Arthralgias
 - Optic neuritis

Rifampin



- ▶ Preparation
 - 150 mg and 300 mg capsules
- ▶ Administration tips
 - Store at room temperature – humidity can affect
 - Powder from capsules can be mixed with liquid or soft food
 - Must be administered immediately after mixing
 - Be careful in opening capsules!

Rifampin



- ▶ Adverse Reactions and Side effects
 - Orange staining of body fluids – fast!
 - Will stain soft contact lens
 - Rash
 - GI upset, flu-like syndrome
 - Liver toxicity
 - Unusual tiredness or loss of appetite
 - Severe abdominal pain
 - Fever chills

Ethambutol

- ▶ Preparation
 - 100 mg and 400 mg tablets
- ▶ Administration tips
 - Store at room temperature
 - Can be taken with food
 - Can be split or crushed and mixed – used immediately



Ethambutol



- ▶ Adverse Reactions and Side effects
 - Visual disturbances – vision changes, blurring, color blindness, trouble seeing, eye pain
 - Swelling of face
 - Rash, hives, trouble breathing
 - Numbness, pain or tingling of hands/feet
 - Joint pain
 - Fever chills
 - Nausea, vomiting, poor appetite, abdominal pain
 - Headaches, dizziness

Pyrazinamide



- ▶ Preparation
 - 500 mg tablets
- ▶ Administration tips
 - Store at room temperature
 - May be taken with food
 - Can be split or crushed
 - Use immediately following mixing with food

Pyrazinamide

- ▶ Adverse Reactions and Side effects
 - Can cause rash after sun exposure – limit sun exposure
 - Gout-like symptoms (pain swelling in joints) and arthralgias
 - GI upset
 - Liver toxicity –
 - yellow skin/dark urine
 - nausea/vomiting
 - Skin rash, severe itching, hives



Rifabutin



- ▶ Preparation
 - 150 mg capsules
- ▶ Administration tips
 - Store at room temperature – humidity can affect
 - Powder from capsules can be mixed with liquids or small amount of food
 - Must be administered immediately after mixing
 - Be careful opening capsules!

Rifabutin

- ▶ Adverse reactions and side effects
 - Rashes and skin discoloration
 - Uveitis and other eye toxicities
 - Liver toxicity similar to rifampin
 - Joint pains
 - Drug interactions



Ethionamide



- ▶ Preparation
 - Coated tablets – 250 mg
- ▶ Administration tips
 - Should be taken with food
 - Client should be on high-dose B6 (pyridoxine) while on drug

Ethionamide

- ▶ Adverse reactions and side effects
 - GI upset and anorexia
 - Metallic taste
 - Hepatotoxicity
 - Endocrine effects – breast enlargement, hair loss, acne, impotence, menstrual issues
 - Neurotoxicity – may be worse if also on cycloserine



Cycloserine

- ▶ Preparation
 - 250 mg capsules
- ▶ Administration tips
 - Best taken on empty stomach – decreases absorption
 - Avoid large amounts of fatty foods
 - Avoid alcohol
 - Must be on high-dose B6(pyridoxine) while on drug



Cycloserine

- ▶ Adverse reactions and toxicity
 - Serious central nervous system effects
 - Inability to concentrate and lethargy
 - Seizures
 - Depression
 - Psychoses
 - Suicidal thoughts
 - Nerve issues in hand/feet
 - Skin changes including rashes, hives



Linezolid (Zyvox)

- ▶ Preparation
 - Coated tablets – 400 mg and 600 mg
 - Intravenous solution
 - Oral powder for suspension
- ▶ Administration tips
 - May be taken with or without food
 - Avoid tyramine containing foods – aged cheeses, dried meats, sauerkraut, soy sauce, tap beers and red wines



Linezolid (Zyvox)

- ▶ Adverse reactions and side effects
 - Visual disturbances
 - Pain, numbness, tingling or weakness in extremities
 - Diarrhea
 - Headache
 - Nausea and vomiting



Levoquin

- ▶ Preparation
 - Coated tablets – 250 mg, 500 mg, 750 mg
 - Solution for injection
 - Oral suspension
- ▶ Administration tips
 - Can be taken with food
 - Drink plenty of beverages
 - Avoid caffeinated foods and beverages
 - May cause sensitivity to sun
 - Do not take within 2 hours of antacids or multivitamins



Levoquin

- ▶ Adverse reactions and toxicities
 - Nausea and bloating
 - Headache
 - Dizziness
 - Insomnia
 - Rare tendon rupture
 - Joint pain
 - Rashes, hives, blistering



Moxifloxacin (Avelox)

- ▶ Preparation
 - Tablets – 400 mg
 - Solution for IV injection
- ▶ Administration tips
 - Keep at room temperature
 - Can be taken with food, but not milk-based products
 - Do not take within 2 hours of antacids or vitamin supplements



Moxifloxacin (Avelox)

- ▶ Adverse reactions and toxicity
 - Nausea and diarrhea
 - Headache and dizziness
 - Rare tendon rupture
 - Rare hepatitis
 - Joint pains



Para-Aminosalicylate (PAS) – Paser

- ▶ Preparation
 - 4 gm packets
- ▶ Administration tips
 - Packets should be kept in refrigerator or freezer
 - Sprinkle over applesauce or yogurt or swirl in acidic juices (tomato, cranberry, apple, or orange)
 - Do not chew
 - May be taken with food
 - Do not use if packet expanded or granules discolored

Para-Aminosalicylate (PAS) – Paser

- ▶ Adverse reactions and toxicity
 - GI upset and diarrhea improve over time
 - Shells of granules may be seen in stool
 - Skin rash, severe itching
 - Nausea, vomiting
 - Unusual tiredness
 - Loss of appetite
 - Black stools or bleeding
 - Rare hepatotoxicity

Capreomycin – Streptomycin Amikacin – Kanamycin

- ▶ Preparation
 - 1 gm vials for reconstitution
 - Vials of solution for injection
- ▶ Administration tips
 - IM or IV use
 - Options for longer term administration



Capreomycin – Streptomycin Amikacin – Kanamycin

- ▶ Adverse reactions and toxicity
 - Kidney toxicity
 - Hearing loss
 - Risk increases with length and age of client
 - May not be reversible
 - Local pain at injection site
 - Electrolyte abnormalities



Treatment in Special Situations

Special Treatment Situations Drug Resistant TB

- ▶ Established only by drug-susceptibility testing
- ▶ Treatment of TB caused by drug-resistant organisms should be done in close consultation with an expert
- ▶ DOT is mandatory for all patients with drug resistant disease

Special Treatment Situations Definitions

- ▶ Primary Drug Resistance
 - Infected with TB which is already drug resistant
 - First susceptibility report will show resistance to one or more anti-TB drugs
- ▶ Secondary Drug Resistance
 - Drug resistance develops during treatment
 - Initial susceptibility report will show sensitive to primary anti-TB drugs
 - Later susceptibility report will show resistance to one or more anti-TB drugs
 - Causes
 - Noncompliance with medications
 - Subtherapeutic regimen – wrong dose
 - Low blood serum levels – lack of absorption
 - Laboratory errors
 - ????

Special Treatment Situations Drug resistant TB

- ▶ Choice of drugs depends on resistance pattern
- ▶ May require second line drug(s)
- ▶ **Requires DOT**
- ▶ Requires >>26 weeks of treatment
- ▶ Almost always requires daily therapy – 5 or 7 days/week
- ▶ Monitoring for culture conversion, clinical improvement, side effects/toxicity critical

Special Treatment Situations The importance of what's missing

- ▶ INH only
 - can treat with rifampin, EMB and PZA for 6 months
 - Fluoroquinolone may help if extensive disease
- ▶ Ethambutol only
 - RIP for 2 months and IR for 4 months – 6 months total
- ▶ PZA only
 - RIE for 2 months and IR for 7 months – 9 months total
- ▶ Rifampin only
 - INH, EMB, fluoroquinolone and PZA for 1st 2 months
 - Total treatment 12–18 months

Special Treatment Situations HIV/AIDS

- ▶ Treatment for HIV-positive patients same as for HIV-negative patients, except :
 - 1) Once-weekly INH-rifapentine in continuation phase is contraindicated in HIV-positive patients
 - 2) Twice-weekly INH-RIF or INH-rifabutin should not be used in patients with CD4+ T-lymphocyte counts less than 100/μl
- ▶ Every effort should be made to use a rifamycin-based regimen for the entire course of therapy

Special Treatment Situations Extrapulmonary TB

- ▶ Similar treatment regimen for pulmonary TB*
- ▶ 6- to 9-month regimens that include INH and RIF are effective
- ▶ Corticosteroids sometimes used as adjunctive therapy for patients with TB meningitis and pericarditis
- ▶ If PZA cannot be used in the initial phase, continuation phase must be increased to ≥ 7 months

Except for central nervous system (CNS) TB, including meningitis; length of therapy is 9-12 months

Special Treatment Situations Pregnancy

- ▶ Untreated TB represents greater hazard to a woman and her child than treatment of disease
- ▶ Treatment of pregnant woman with suspected TB should be started if probability of TB is moderate to high

Special Treatment Situations Pregnancy

- ▶ Initial phase treatment regimen should consist of INH, RIF, and EMB
- ▶ PZA not generally recommended for pregnant women in the United States
- ▶ SM should not be substituted for EMB because of possible teratogenic effects

Special Treatment Situations: Renal Insufficiency and End-Stage – Renal Disease

- ▶ Renal insufficiency complicates management of TB because some antituberculosis medications are cleared by the kidneys
- ▶ Dosage should not be decreased because peak serum concentrations may be too low; smaller doses may decrease drug efficacy

Special Treatment Situations Renal Insufficiency and End-Stage Renal Disease

- ▶ Dosing interval of antituberculosis drugs should be increased
- ▶ Most drugs can be given 3 times weekly after hemodialysis; for some drugs, dose must be adjusted

Special Treatment Situations Hepatic Disease

- ▶ May need to consider regimens with fewer hepatotoxic agents for patients with liver disease
- ▶ Recommended regimens:
 - 1) Treatment without PZA
Initial phase (2 months): INH, RIF, and EMB
Continuation phase (7 months): INH and RIF
 - 2) Treatment without INH
Initial phase (2 months): RIF, PZA, and EMB
Continuation phase (4 months): RIF, EMB, and PZA

Special Treatment Situations Hepatic Disease

- Recommended regimens: (continued)
 - 3) Regimens with only one potentially hepatotoxic drug
 - RIF should be retained
 - Duration of treatment is 12-18 months
 - 4) Regimens with no potentially hepatotoxic drugs
 - Duration of treatment is 18-24 months

Treatment Guidelines Online

- ▶ CDC Treatment of Tuberculosis Guidelines:
<http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf>
- ▶ New Core Curriculum on Tuberculosis: What the Clinician Should Know
<http://www.cdc.gov/tb/education/corecurr/default.htm>

Monitoring and Other Issues

Treatment Monitoring

- ▶ Periodic (minimum monthly) clinical evaluation to assess adherence and identify adverse reactions
- ▶ Bacteriologic monitoring
 - Sputum to assess early response until smear negative
 - After converted to smear negative, monthly sputum clusters (3) until culture negative
 - Obtain additional drug-susceptibility tests if patient remains culture-positive after 3 months of treatment
 - Also medical evaluation, possible drug serum levels

Treatment Monitoring

- ▶ Repeat chest x-rays generally not indicated
- ▶ Follow-up films may be needed:
 - At completion of initial treatment phase for patients with initial negative cultures to establish clinical diagnosis
 - At end of treatment to establish a new baseline
 - Individuals with extensive TB disease or who are HIV-infected

Treatment Monitoring

- ▶ Repeat blood work if abnormalities at baseline or symptoms appear
 - Follow local district protocol
 - Lab monitoring changes for second line drugs
 - Varies with specific drugs used
- ▶ Visual acuity and color vision monthly if EMB used
- ▶ Hearing screening required for ototoxic drugs
 - Think injections

Types of Adverse Effects

- ▶ Side Effect – Uncomfortable but not dangerous effect of medications as properly administered
 - Most meds – nausea, other GI symptoms
 - usually can continue treatment – can be sign/symptom of hepatitis
 - Diarrhea less common but potentially important – can be marker for malabsorption, predict low blood/tissue drug levels
 - First line meds – non-specific itching
 - Itching, non-specific rashes common – can be initial sign of hepatitis
 - Hives, extensive maculo-papular, purpura rare – require D/C meds, contact HCP, consider ER

Types of Adverse Effects

- CNS/peripheral nervous system side effects
 - Irritability, sleepiness, insomnia common
 - Peripheral neuropathy – usually isoniazid; pyridoxine prevents
 - Optic neuritis – causes visual disturbances
 - feared w/ ethambutol, can be seen w/ other meds
- ▶ Musculoskeletal –
 - PZA can cause non-specific muscle and joint pain
 - PZA elevates uric acid – can induce gout
- ▶ “Flu-like” symptoms – can occur w/ rifampin
 - more common twice weekly treatment
- Report to case manager immediately

Types of Adverse Effects

- ▶ Toxicity – Adverse effect on metabolic processes (e.g., enzyme systems, tissue replication or repair mechanisms); often dose related
 - INH – hepatitis, peripheral neuropathy
 - Rifampin – hepatitis
 - Ethambutol – retrobulbar neuritis
 - Aminoglycosides – ototoxicity, nephrotoxicity

Common Adverse Reactions to Drug Treatment

Caused by	Adverse Reaction	Signs and Symptoms
Any drug	Allergy	Skin rash
Ethambutol	Eye damage	Blurred or changed vision Changed color vision
Isoniazid, Pyrazinamide, or Rifampin	Hepatitis	Abdominal pain Abnormal liver function test results Fatigue Lack of appetite Nausea / Vomiting Yellowish skin or eyes Dark urine

Common Adverse Reactions to Drug Treatment

Caused by	Adverse Reaction	Signs and Symptoms
Isoniazid	Peripheral neuropathy	Tingling sensation in hands and feet
Pyrazinamide	Gastrointestinal intolerance Arthralgia Arthritis	Upset stomach, vomiting, lack of appetite Joint aches Gout (rare)
Streptomycin	Ear damage Kidney damage	Balance problems Hearing loss Ringing in the ears Abnormal kidney function test results

Common Adverse Reactions to Drug Treatment

Caused by	Adverse Reaction	Signs and Symptoms
Rifamycins	Thrombocytopenia	Easy bruising
Rifabutin		Slow blood clotting
Rifapentine	Gastrointestinal intolerance	Upset stomach
Rifampin	Drug interactions	Interferes with certain medications, such as birth control pills, birth control implants, and methadone treatment

Other TB Drug Effects

- ▶ Drug-drug interactions
 - May increase or decrease effective dose of either TB drug or other medication
 - Rifamycins
 - Rapid metabolism of methadone, warfarin, theophylline – may require increased doses
 - INH
 - May decrease concentrations of phenytoin, diazepam – require increased doses

When to Extend Continuation Phase of Treatment

- ▶ Treatment increased to 9 months total duration
 - from 2 drugs x 4 months to 2 drugs x 7 months
 - Recommended for patients with cavitary pulmonary disease **and** positive 2-month sputum culture
 - Extension may be considered if either factor is present
 - Initial phase did not include PZA

Miscellaneous Comments

- Difficulty swallowing pills
 - Patient may not tell you
 - Crushed pills, administered in small amt food ok
 - Make sure they will finish amount you use!
 - Teach how to swallow meds
 - Tablets SINK – TILT HEAD UP
 - Capsules FLOAT – TIL HEAD DOWN

Summary

- ▶ TB is treated with multiple drugs for a prolonged period of time
- ▶ Drug resistance generally extends treatment – length depends on missing drug(s)
- ▶ All anti-TB drugs have side effects and toxicities
- ▶ Second-line drug side effects are usually worse
- ▶ Regular monitoring for side effects and toxicities is critical!