

Module 4: Treatment of Latent Tuberculosis Infection and Tuberculosis Disease

Slide 1: (Title Slide.) Self- Study Modules on Tuberculosis, Module 4, Treatment of Latent Tuberculosis Infection and Tuberculosis Disease

Slide 2: Module 4: Objectives

At completion of this module, learners will be able to:

1. List groups of people who should receive high priority for latent TB infection (LTBI) treatment
2. Describe treatment regimens for LTBI
3. Describe treatment regimens for TB disease
4. Describe principles of preventing drug resistance
5. Describe patient monitoring during LTBI and TB disease treatment
6. Describe TB treatment adherence strategies
7. List common adverse reactions to drugs used to treat LTBI and TB disease

Slide 3: Module 4: Overview

- Treatment of LTBI
 - Patient Medical Evaluation
 - LTBI Treatment Regimens
 - Special Considerations for LTBI Treatment
- Treatment of TB Disease
 - TB Disease Treatment Regimens

Slide 4: Overview (cont.)

- Treatment of TB Disease (cont.)
 - Special Considerations and Alternative Treatment Regimens
 - Treatment and Monitoring Plan and Adverse Reactions
 - Adherence and Evaluating Patients' Response to Treatment
 - Role of Public Health Workers
- Case Studies

Slide 5: (Title Slide.) Treatment of Latent TB Infection (LTBI)

Slide 6: Treatment of LTBI (1)

- LTBI is treated to prevent the development of TB disease
- LTBI is treated with medication

Slide 7: Treatment of LTBI (2)

- Targeted testing should be used to identify and treat people who are:
 - At high risk for exposure to or infection with *M. tuberculosis*
 - At high risk for developing TB disease once infected with *M. tuberculosis*
- People in these groups should receive high priority for LTBI treatment if they have a positive tuberculin skin test (TST) or interferon-gamma release assay (IGRA)

Slide 8: High Priority for LTBI Treatment (1)

- High-priority groups for LTBI treatment if positive IGRA or TST result of ≥ 5 mm
 - Recent contacts of people with infectious TB disease

- People living with HIV
- People with chest x-ray findings suggestive of previous TB disease
- Patients with an organ transplant
- Other immunosuppressed patients

Slide 9: High Priority for LTBI Treatment (2)

- High-priority groups for LTBI treatment if positive IGRA or TST result of ≥ 10 mm:
 - People who have come to U.S. from countries where TB is common
 - People who abuse drugs
 - People who live or work in high-risk congregate settings
 - People who work in mycobacteriology laboratories

Slide 10: High Priority for LTBI Treatment (3)

- High-priority groups for LTBI treatment if positive IGRA or TST result of ≥ 10 mm (cont.):
 - People with medical conditions that increase risk of TB disease
 - Children younger than 5 years of age
 - Infants, children, and adolescents exposed to adults in high-risk groups

Slide 11: Low Priority for LTBI Treatment

- Individuals without any risk factors generally should not be tested for TB infection
- However, individuals with no risk factors who are tested and have a positive IGRA or TST result of ≥ 15 mm should be evaluated for LTBI treatment

Slide 12: (Title Slide.) Treatment of Latent TB Infection (LTBI): Patient Medical Evaluation

Slide 13: Patient Medical Evaluation (1)

- Medical evaluations should be done to:
 1. Exclude possibility of TB disease
 2. Determine whether patient has ever been treated for TB infection or TB disease
 3. Find out if patient has any medical conditions that may complicate therapy
 4. Establish and build rapport with patient

Slide 14: Patient Medical Evaluation (2)

- 1. Exclude possibility of TB disease
 - Treating TB disease with LTBI treatment regimen can lead to drug resistance
 - Clinicians should determine if the patient has symptoms of TB disease
 - Clinicians should evaluate the patient with a chest x-ray
 - Patients with symptoms or chest x-ray findings of TB disease should be given TB disease treatment, not LTBI treatment

Slide 15: Patient Medical Evaluation (3)

- 2. Determine whether patient has ever been treated for TB infection or TB disease
 - Patients who have been adequately treated should not be treated again
 - TST or IGRA results cannot determine if patient has received treatment for LTBI or TB disease; or if they have been re-infected after treatment

Slide 16: Patient Medical Evaluation (4)

- 3. Find out if patient has any medical conditions that may complicate therapy or require more careful monitoring. These patients include:

- People living with HIV
- People with history of liver disorder or disease
- People who use alcohol regularly
- Women who are pregnant or just had a baby (within 3 months of delivery)
- People who are taking other medications that may increase the risk of hepatitis

Slide 17: Patient Medical Evaluation (5)

- For patients with the medical conditions listed on the previous slide, baseline laboratory liver function tests (to detect injury to liver) are recommended before starting LTBI treatment.

Slide 18: Patient Medical Evaluation (6)

- It is important to find out if:
 - Patient has ever had adverse reactions to LTBI drugs
 - Patient is currently on medications that may interact with LTBI drugs
- [IMAGE: Doctor talking to a patient.]

Slide 19: Patient Medical Evaluation (7)

- **4. Establish and build rapport with patient**
 - Health care workers (HCWs) should highlight important aspects of treatment, such as:
 - Benefits of treatment
 - Importance of adherence to treatment
 - Possible adverse reactions
 - Establishment of a follow-up plan

Slide 20: Patient Medical Evaluation (8)

- Because of the interaction between TB and HIV, HCWs should also recommend that patients undergo HIV counseling and testing

Slide 21: (Title Slide.) Treatment of Latent TB Infection (LTBI): LTBI Treatment Regimens

Slide 22: LTBI Treatment Regimens (1): Isoniazid

- Isoniazid (INH) daily for 9 months is very effective in preventing the development of TB disease
- INH may also be given for 6 months
 - Cost effective and patients may find it easier to adhere, BUT:
 - Not as effective if given for less than 6 months
 - Not recommended for people living with HIV, individuals with previous TB disease, or children

Slide 23: LTBI Treatment Regimens (2): Isoniazid and Rifapentine (12-Dose Regimen)

- Combination of INH and rifapentine (RPT) given in 12, once-a-week doses under DOT, if possible
- Recommended for patients who:
 - Are 12 years of age or older
 - Were recently exposed to infectious TB
 - Have a TST or IGRA conversion from negative to positive
 - Have chest x-ray findings of previous TB disease
- Regimen may be used in otherwise healthy HIV-infected persons who are:
 - 12 years of age or older

- Not on antiretroviral therapy (ART), except those taking an efavirenz or raltegravir-based ART regimen

Slide 24: LTBI Treatment Regimens (3): Isoniazid and Rifapentine (12-Dose Regimen)

- This regimen is not recommended for
 - Children younger than 2 years of age
 - People with HIV/AIDS who are taking certain ART regimens
 - People presumed to be infected with isoniazid or rifampin-resistant *M. tuberculosis*
 - Pregnant women or women expecting to become pregnant within the 12-week regimen

Slide 25: LTBI Treatment Regimens (4): Rifampin

- Rifampin (RIF) is also recommended for people with a positive TST or IGRA result
 - Especially if the person has been exposed to INH-resistant TB
- RIF should be given daily for 4 months
- RIF should not be used with certain combinations of ART
- In some cases, rifabutin (RFB) may be substituted when RIF cannot be used

Slide 26: LTBI Treatment Regimens (5): Rifampin and Pyrazinamide

- CDC advises against using a combination of RIF and pyrazinamide (PZA) due to serious side effects such as:
 - Severe liver injury
 - Death

Slide 27: LTBI Treatment Regimens (6)

- [IMAGE: Please reference Table 4.2 LTBI Treatment Regimens, in Module 4, pgs. 8-9 (pdf) www.cdc.gov/tb/education/ssmodules/pdfs/tb_selfstudymodules_2015_module04.pdf]

Slide 28: LTBI Treatment Regimens (7)

- [IMAGE: Please reference Table 4.2 LTBI Treatment Regimens, in Module 4, pgs.8- 9 (pdf) www.cdc.gov/tb/education/ssmodules/pdfs/tb_selfstudymodules_2015_module04.pdf]

Slide 29: Treatment of LTBI: Study Question 4.1

- What is the purpose of LTBI treatment?
 - To prevent people with latent TB infection from developing TB disease.

Slide 30: Treatment of LTBI: Study Question 4.2

- Which groups of people should receive high-priority for LTBI treatment if they have a positive IGRA or TST result of ≥ 5 mm? Name 5.
 - Recent contacts of people with infectious TB disease
 - People living with HIV
 - People with chest x-ray findings suggestive of previous TB disease
 - Patients with an organ transplant
 - Other immunosuppressed patients

Slide 31: Treatment of LTBI: Study Question 4.3

- Which groups of people should receive high priority for LTBI treatment if they have a positive IGRA result or a TST reaction that is ≥ 10 mm? Name 7.
 - People who come to the U.S. from areas of the world where TB is common
 - People who abuse drugs

- People who live or work in high-risk congregate settings
- People who work in mycobacteriology laboratories
- People with medical conditions that increase risk of TB disease
- Children younger than 5 years of age
- Infants, children, and adolescents exposed to adults in high-risk groups

Slide 32: LTBI Treatment Regimens: Study Question 4.4

- List 4 regimens that are approved for the treatment of LTBI.
 - Isoniazid for 9 months
 - Isoniazid for 6 months
 - Isoniazid and rifapentine for 12, once-weekly doses (12-dose regimen)
 - Rifampin for 4 months

Slide 33: (Title Slide.) Treatment of Latent TB Infection (LTBI): Special Considerations for LTBI Treatment

Slide 34: Special Considerations for LTBI (1): Directly Observed Therapy (DOT)

- DOT is when a HCW or another designated person watches a patient swallow each dose of medication
 - Used to help patients adhere to treatment
 - Should be considered for people who are at high risk for TB or suspected to be non-adherent
 - Recommended for intermittent therapy

Slide 35: Special Considerations for LTBI (2): Contacts

- Contacts are people who have been exposed to someone with infectious TB disease
- Contacts should be quickly identified, located, and assessed for LTBI and TB disease
 - If TST or IGRA result is positive, contacts should be given high priority for LTBI treatment (once TB disease is ruled out)
 - If TST or IGRA result is negative, contacts should be retested in 8 to 10 weeks

Slide 36: Special Considerations for LTBI (3): Contacts

- In general, contacts with positive test result and a documented history of completion of LTBI treatment do not need to be retreated
- However, retreatment may be necessary for persons at high risk of:
 - Becoming re-infected
 - Progressing to TB disease

Slide 37: Special Considerations for LTBI (4): Contacts at High Risk for Rapid Development of TB Disease

- Some contacts may be started on LTBI treatment even if their test result is negative, and less than 8 to 10 weeks have passed since last exposure to TB; this includes:
 - Children younger than 5 years of age
 - People living with HIV
- Expert consultation should be sought to determine if contacts with immunocompromised states other than HIV infection could benefit from treatment even if they have a negative TST or IGRA result

Slide 38: Special Considerations for LTBI (5): Contacts at High Risk for Rapid Development of TB Disease

- Once active TB disease is ruled out, contacts at high risk for TB disease should:
 - Start LTBI treatment
 - Be retested 8 to 10 weeks after last exposure to TB
 - If negative test result: stop LTBI treatment
 - If positive test result: continue LTBI treatment
 - Contacts living with HIV may be given full course of LTBI treatment even if their second TST or IGRA result is negative

Slide 39: Special Considerations for LTBI (6): Infants and Children

- Infants and children are more likely to develop life-threatening forms of TB disease
- Children younger than 5 years of age who have been exposed to TB should start taking LTBI treatment even if they have a negative TST or IGRA result because they:
 - Are at high risk for rapidly developing TB disease
 - May have a false-negative TST reaction

Slide 40: Special Considerations for LTBI (7): Infants and Children

- Infants and children should be retested 8 to 10 weeks after last exposure
- LTBI treatment can be stopped if ALL of the following conditions are met:
 - Child is at least 6 months of age
 - Second TST or IGRA is negative
 - Second TST or IGRA was done at least 8 weeks after child was last exposed to a person with infectious TB disease
 - The 12-dose regimen is not recommended for children younger than 2 years of age

Slide 41: Special Considerations for LTBI (8): Contacts of INH-Resistant TB

- Contacts of patients with INH-resistant, but RIF-susceptible TB, may be treated with a 4-month daily regimen of RIF
- In some patients, rifabutin (RFB) may be substituted if RIF cannot be used

Slide 42: Special Considerations for LTBI (9): Contacts of Multidrug-Resistant TB (MDR TB)

- The risk for developing TB disease should be considered before recommending LTBI treatment
- Contacts of patients with MDR TB
 - May be treated for 6 to 12 months with an alternative regimen of drugs to which the *M. tuberculosis* isolate is susceptible
 - Can be observed for signs and symptoms of TB disease without treatment
- All persons with suspected MDR LTBI should be followed and observed for signs and symptoms of TB disease for 2 years, regardless of the treatment regimen

Slide 43: Special Considerations for LTBI (10): Pregnant Women

- For most pregnant women, LTBI treatment can be delayed until after delivery, unless they have certain risk factors
- Immediate treatment should be considered if woman is living with HIV or is a recent TB contact
- Preferred LTBI treatment regimen is 9 months of INH with a vitamin B6 supplement
 - INH has not been shown to have harmful effects on the fetus
- The 12-dose regimen is not recommended for pregnant women or women expecting to become pregnant within the 12-week regimen

Slide 44: Special Considerations for LTBI (11): Breastfeeding Women

- Women who are breastfeeding can take INH, but should also be given a vitamin B6 supplement
- Amount of INH in breast milk is not enough to be considered treatment for infant
- [IMAGE: Woman holding an infant.]

Slide 45: Special Considerations for LTBI (12): People Living with HIV

- Individuals living with HIV should be treated with 9-month regimen of INH
- RIF should not be used for people who are taking certain combinations of ART
 - Dose-adjusted rifabutin (RFB) may be given
- The 12-dose regimen of INH and RPT may be used for people living with HIV who are:
 - 12 years of age or older
 - Not on ART, except those taking an efavirenz or raltegravir-based ART regimen

Slide 46: LTBI Treatment Regimens: Study Question 4.5

- What LTBI treatment regimen may be recommended for people with a positive TST or IGRA result who have been exposed to INH-resistant TB?
 - Treatment with rifampin for 4 months may be recommended in this situation.

Slide 47: Special Considerations for LTBI Study Question 4.6

- In what circumstances may LTBI treatment be given to people who have a negative TST or IGRA result?
 - Some contacts may start LTBI treatment if they have a negative TST or IGRA, but less than 8 to 10 weeks have passed since last exposed to TB; these contacts include:
 - Children who are younger than 5 years of age
 - People living with HIV

Slide 48: Special Considerations for LTBI: Study Question 4.7

- What conditions must be met to stop LTBI treatment for children who are younger than 5 years of age and have been exposed to TB?
 - LTBI treatment can be stopped if ALL the following conditions are met:
 - Child is at least 6 months of age
 - Second TST or IGRA is negative
 - Second TST or IGRA was done 8 to 10 weeks after the child was last exposed to TB

Slide 49: Special Considerations for LTBI: Study Question 4.8

- When should pregnant women be treated for LTBI and for how long?
 - For most pregnant women with TB infection, LTBI treatment can be delayed until after delivery. If the pregnant woman is HIV-infected or a recent contact, immediate treatment should be considered.
 - Preferred treatment regimen for pregnant women is 9 months of INH with a vitamin B6 supplement.

Slide 50: (Title Slide.) Treatment of Latent TB Infection (LTBI): Adverse Reactions and Patient Monitoring

Slide 51: Adverse Reactions to INH (1)

- About 10% to 20% of people treated with INH will have mild, abnormal liver test results during treatment
 - In most people, liver test results return to normal

Slide 52: Adverse Reactions to INH (2): Hepatitis

- A major risk of INH is hepatitis (inflammation of the liver)
- Hepatitis prevents the liver from functioning normally, causing symptoms such as:
 - Nausea
 - Vomiting
 - Abdominal pain
 - Fatigue
 - Brown urine

Slide 53: Adverse Reactions to INH (3): Hepatitis

- INH can cause hepatitis in anyone; however, hepatitis occurs in less than 1% of people taking INH
- Certain risk factors increase the risk of serious hepatitis, such as:
 - Older age
 - Alcoholism

Slide 54: Adverse Reactions to INH (4): Peripheral Neuropathy

- INH can cause peripheral neuropathy
 - Damage to sensory nerves of hands and feet
 - Symptoms include a tingling sensation, weakened sense of touch, or pain in the hands, palms, soles and feet
- HIV, alcoholism, diabetes, and malnutrition increase risk for peripheral neuropathy
 - People with these conditions should be given vitamin B6

Slide 55: Adverse Reactions to RIF, RPT, and RFB

- Hepatitis is more likely to occur when RIF is combined with INH
- Other side effects of RIF, RPT, and RFB include:
 - Rash
 - Gastrointestinal symptoms
 - Orange discoloration of urine, saliva, and tears
 - Interaction with many other drugs, such as birth control pills and implants, warfarin, some HIV drugs, and methadone
 - Hypersensitivity

Slide 56: Adverse Reactions to RPT and RFB

- RPT may cause flu-like symptoms
- RFB may cause
 - Eye inflammation
 - Joint pain
 - Lower white blood cell count

Slide 57: Adverse Reactions

- Patients should be instructed to report any signs and symptoms of adverse drug reactions to their health care provider
- Patients should stop taking the medication and seek medical attention immediately if symptoms of serious adverse reactions occur
 - No appetite
 - Nausea

- Vomiting
- Yellowish skin or eyes
- Fever for 3 or more days
- Abdominal pain
- Tingling in fingers and toes
- Brown urine

Slide 58: Patient Monitoring (1)

- All persons taking LTBI treatment should be educated about symptoms caused by adverse reactions
- Patients need to be evaluated at least monthly during therapy for:
 - Adherence to prescribed regimen
 - Signs and symptoms of TB disease
 - Adverse reactions

Slide 59: Patient Monitoring (2)

- During each monthly evaluation, patients should be:
 - Asked whether they have nausea, abdominal pain, or other symptoms of adverse reactions
 - Examined by HCW for adverse reactions
 - Instructed to stop medications and contact HCWs immediately if they have signs or symptoms of hepatitis

Slide 60: Patient Monitoring (3)

- People at greatest risk for hepatitis should have baseline liver function tests before starting LTBI treatment and every month during therapy. This includes:
 - People living with HIV
 - People with history of liver disorder or disease
 - People who use alcohol regularly
 - Women who are pregnant or just had a baby
 - People taking medications that may increase risk of hepatitis

Slide 61: Patient Monitoring (4)

- For all patients, INH, RIF, and RPT should be stopped if liver function test results are:
 - 3 times higher than upper limit of the normal range and patient has symptoms
 - OR
 - 5 times higher than upper limit of the normal range and patient has no symptoms

Slide 62: LTBI Treatment Follow-Up

- Patients should receive documentation of TST or IGRA results, treatment regimens, and treatment completion dates
 - Patients should present these documents any time they are required to be tested for TB infection
- Patients should be re-educated about signs and symptoms of TB disease

Slide 63: Medical Evaluation: Study Question 4.9

- Name 4 reasons why patients should receive a medical evaluation before starting LTBI treatment.
 - Exclude possibility of TB disease

- Determine whether they have ever been treated for TB infection or TB disease
- Identify any medical conditions that may complicate therapy or require more careful monitoring
- Establish and build rapport with patient

Slide 64: LTBI Treatment: Study Question 4.10

- Why is it important to exclude the possibility of TB disease before giving a patient LTBI treatment?
 - Treating TB disease with LTBI treatment regimen (usually a single drug) can lead to drug resistance

Slide 65: Adverse Reactions: Study Question 4.11

- What are the symptoms of hepatitis?
 - Nausea
 - Vomiting
 - Abdominal pain
 - Fatigue
 - Brown urine

Slide 66: Adverse Reactions: Study Question 4.12

- People with greatest risk for hepatitis are:
 - People living with HIV
 - People with a history of liver disorder or disease
 - People who use alcohol regularly
 - Women who are pregnant or just had a baby
 - People who are taking other medications that may increase the risk of hepatitis
- These patients should have liver function tests before starting LTBI treatment and during therapy

Slide 67: Adverse Reactions: Study Question 4.13

- How often should patients be evaluated for signs and symptoms of adverse reactions during LTBI treatment?
 - All patients receiving LTBI treatment should be evaluated at least monthly during therapy.

Slide 68: (Title Slide.) Treatment of TB Disease

Slide 69: Treatment of TB Disease (1)

- Treating TB disease benefits both the person who has TB and the community
 - Patient: prevents disability and death; restores health
 - Community: prevents further transmission of TB
- TB disease must be treated for at least 6 months; in some cases, treatment lasts longer

Slide 70: Treatment of TB Disease (2)

- Intensive Phase
 - First 8 weeks of treatment
 - Most bacilli killed during this phase
 - 4 drugs used
- Continuation Phase
 - After first 8 weeks of TB disease treatment

- Bacilli remaining after intensive phase are treated with at least 2 drugs
- Relapse
 - Occurs when treatment is not continued for long enough
 - Surviving bacilli may cause TB disease at a later time

Slide 71: Treatment of TB Disease (3)

- Intensive phase should contain the following four drugs:
 - Isoniazid (INH)
 - Rifampin (RIF)
 - Pyrazinamide (PZA)
 - Ethambutol (EMB)
- **[IMAGE: Example of pills used to treat TB disease. From left to right: isoniazid, rifampin, pyrazinamide, and ethambutol.]**

Slide 72: Treatment of TB Disease (4)

- Treatment must contain multiple drugs to which organisms are susceptible
- Treatment with a single drug can lead to the development of drug-resistant TB

Slide 73: Preventing Drug Resistance (1)

- Drug resistance can develop when patients are prescribed an inappropriate regimen
 - TB disease must be treated with at least 2 drugs to which bacilli are susceptible
 - Using only one drug can create a population of tubercle bacilli resistant to that drug
 - Adding a single drug to failing regimen may have the same effect as only using one drug

Slide 74: Preventing Drug Resistance (2)

- Resistance can develop when patients do not take drugs as prescribed
 - Patients do not take all of their pills
 - Patients do not take pills as often as prescribed
 - When this happens, patients may expose the bacilli to a single drug

Slide 75: Preventing Drug Resistance (3)

- Factors that increase the chance of patient having or developing drug-resistant TB:
 - Patient does not take their medicine regularly and completely
 - Patient comes from an area of the world where drug-resistant TB is common
 - Malabsorption of drugs
 - Patient is a contact to someone with drug-resistant TB
 - Failure to improve on drug-susceptible regimen
 - Patient develops TB disease again after having taken TB medicine in the past

Slide 76: (Title Slide.) Treatment of TB Disease: Treatment Regimens

Slide 77: TB Treatment Regimens

- **[IMAGE: Please reference Table 4.3 Drug Regimens for Pulmonary TB Caused by Drug Susceptible Organisms in Adults, in Module 4, pg. 24 (pdf)**
www.cdc.gov/tb/education/ssmodules/pdfs/tb_selfstudymodules_2015_module04.pdf

Slide 78: Treatment of TB Disease: Study Question 4.14

- Why must TB disease be treated for at least 6 months?

- Even though most bacilli are killed in the first 8 weeks, some bacilli can survive. Therefore, treatment must continue in order to kill all remaining bacilli.

Slide 79: Treatment of TB Disease: Study Question 4.15

- Which 4 drugs are recommended for the intensive phase of treatment for TB disease?
 - The intensive phase should include isoniazid, rifampin, pyrazinamide, and ethambutol.

Slide 80: Treatment of TB Disease: Study Question 4.16

- Why should multiple drugs be used to treat TB disease?
 - Using only one drug can create a population of tubercle bacilli that is resistant to that drug. When multiple drugs are used together, each drug helps prevent the emergence of bacilli that are resistant to the other drugs.

Slide 81: Drug Resistance: Study Question 4.17

- Name 2 factors that can lead to drug resistance.
 - Drug resistance can develop when:
 - Patients are prescribed an inappropriate regimen for treatment
 - Patients do not follow treatment regimens as prescribed

Slide 82: (Title Slide.) Treatment of TB Disease: Special Considerations

Slide 83: Special Considerations (1)

- TB medical experts should be consulted for complicated and challenging TB treatment issues
- Consultation can be provided by State TB Programs and the CDC-funded TB Regional Training and Medical Consultation Centers (RTMCCs) www.cdc.gov/TB/education/rtmc/default.htm

Slide 84: Special Considerations (2): People Living with HIV

- For HIV-infected TB patients receiving ART, the recommended treatment is a 6-month daily regimen consisting of:
 - An intensive phase of INH, RIF, PZA, and EMB for 2 months
 - A continuation phase of INH and RIF for 4 months

Slide 85: Special Considerations (3): People Living With HIV

- ART should be initiated during TB treatment to improve treatment outcomes for TB patients living with HIV
- ART should ideally be initiated
 - Within 2 weeks of starting TB treatment for patients with CD4 cell counts $<50/\text{mm}^3$
 - By 8 to 12 weeks of starting TB treatment for patients with CD4 cell counts $>50/\text{mm}^3$
- For patients with TB meningitis or TB involving the central nervous system, ART should NOT be initiated during the first 8 weeks of TB treatment

Slide 86: Special Considerations (4): People Living With HIV

- It is important to be aware of the interaction of RIF with some ART drugs
 - Rifabutin has fewer drug interaction problems and may be used as a substitute for RIF for some patients
- DOT should be provided for all TB patients living with HIV
- For patients not receiving ART during TB treatment, it is recommended to extend treatment to 9 months

Slide 87: Special Considerations (5): Pregnant Women

- Treatment should begin as soon as TB disease is diagnosed
- Regimen should consist of at least INH, RIF, and EMB for a minimum of 9 months
- Clinicians should seek expert consultation to evaluate the risks and benefits of prescribing pyrazinamide (PZA) on a case-by-case basis
- Streptomycin (SM) should NOT be used
- Vitamin B6 supplements are recommended for all pregnant women taking INH

Slide 88: Special Considerations (6): Breastfeeding

- Women being treated with first-line TB drugs should not be discouraged from breastfeeding
 - Only a small concentration of the drugs is found in breast milk
 - Not harmful to infant

Slide 89: Special Considerations (7): Breastfeeding

- Concentration of drugs in breast milk is not considered effective treatment for LTBI or TB disease for infant
- Vitamin B6 supplements are recommended for all women who are taking INH and are breastfeeding

Slide 90: Special Considerations (8): Children

- Children younger than 5 years of age should start TB treatment as soon as the diagnosis is suspected
- Children can be treated with INH, RIF, PZA, and EMB for 2 months, followed by INH and RIF for 4 months
 - Children receiving EMB should be monitored for vision changes
 - A 3 drug regimen (INH, RIF, PZA) can be considered in the intensive phase for children who are too young to have their vision monitored, are not infected with HIV, have no prior TB treatment history, and are not at risk for having drug-resistant TB

Slide 91: Special Considerations (9): People with Extrapulmonary Disease

- In general, regimens used for treating pulmonary TB are also effective for treating extrapulmonary TB
- 9 to 12 month regimen is recommended for TB of the meninges or central nervous system
- 6 to 9 month regimen is recommended for bone and joint TB

Slide 92: (Title Slide.) Treatment of TB Disease: Alternative Regimens for Treating Drug-Resistant TB

Slide 93: Alternative Treatment Regimens (1): Drug-Resistant TB

- Alternative regimens should be used for treating drug-resistant TB
- Treatment of drug-resistant TB should always be done under the supervision of a medical expert

Slide 94: Alternative Treatment Regimens (2): Drug-Resistant TB

- INH-resistant TB can be treated with the following regimen:
 - RIF, EMB, and PZA for 6 months

Slide 95: Alternative Treatment Regimens (3): MDR TB

- MDR TB is resistant to INH and RIF, and is more difficult to treat than drug-susceptible TB
- Drugs that can be used are less effective and are more likely to cause adverse reactions

- Treatment can last 18 to 24 months after culture conversion
- As a last resort, some patients undergo surgery to remove part of the disease site
- Expert consultation should be sought

Slide 96: Alternative Treatment Regimens (4): Extensively Drug-Resistant TB (XDR TB)

- XDR TB is resistant to INH, RIF, plus any fluoroquinolone, and at least one injectable second-line drug (e.g., amikacin, kanamycin, or capreomycin)
- XDR TB patients have less effective treatment options
- XDR TB is very difficult to treat
- Expert consultation should be sought

Slide 97: Alternative Treatment Regimens (5): XDR TB

- Successful outcomes for the patient depend greatly on:
 - Extent of drug resistance
 - Severity of disease
 - Whether the patient's immune system is compromised

Slide 98: Special Considerations: Study Question 4.18

- What treatment regimen should be used for HIV-infected TB patients?
 - 6-month daily regimen consisting of an intensive phase of INH, RIF, PZA, and EMB for 2 months followed by a continuation phase of INH and RIF for 4 months
 - ART should ideally be initiated
 - Within 2 weeks of starting TB treatment for patients with CD4 cell counts $<50/\text{mm}^3$
 - By 8 to 12 weeks of starting TB treatment for patients with CD4 cell counts $\geq 50/\text{mm}^3$
 - For patients with TB meningitis or TB involving the central nervous system, ART should NOT be initiated during the first 8 weeks of TB treatment

Slide 99: Special Considerations: Study Question 4.19

- In what situations should treatment for TB disease last longer than the usual course of treatment?
 - HIV-infected TB patients need a minimum of 6 months of treatment. If an HIV-infected patient is NOT receiving ART during TB treatment, it is recommended to prolong treatment to 9 months.
 - Pregnant women with TB disease should receive at least 9 months of treatment
 - Persons with TB disease of the meninges or central nervous system should receive a 9 to 12-month regimen
 - Persons with bone or joint TB disease should receive a 6 to 9-month regimen
 - Extending treatment should be considered for patients with TB disease in any site that is slow to respond
 - Treatment for MDR TB disease can last 18 to 24 months

Slide 100: (Title Slide.) Treatment of TB Disease: Treatment and Monitoring Plan and Adverse Reactions

Slide 101: Treatment and Monitoring Plan: TB Disease

- Every TB patient should have a specific treatment and monitoring plan developed in collaboration with local health department
- Plan should include:

- Description of treatment regimen
- Methods of:
 - Monitoring for adverse reactions
 - Assessing and ensuring adherence to treatment
 - Evaluating treatment response

Slide 102: Monitoring Adverse Reactions (1): TB Disease

- Before starting treatment for TB disease, patients should have baseline blood and vision tests to detect problems that may complicate treatment
 - For example, patients who are taking ethambutol should have baseline visual acuity testing and testing of color discrimination

Slide 103: Monitoring Adverse Reactions (2): TB Disease

- Follow-up tests should be done periodically if:
 - Results of baseline tests indicate abnormalities
 - Patient has symptoms that may be due to adverse reactions

Slide 104: Monitoring Adverse Reactions (3): TB Disease

- Patients should be educated about symptoms caused by adverse reactions to drugs
- Patients should be seen by clinician at least monthly during treatment and evaluated for possible adverse reactions
- Public health workers who have regular contact with patients should ask about adverse reactions to treatment

Slide 105: Monitoring Adverse Reactions (4): TB Disease

- If patient has symptoms of a serious adverse reaction, HCWs should:
 - Instruct patient to stop medication
 - Report situation to clinician and arrange for medical evaluation
 - Note symptoms on the patient's form
- [IMAGE: Health care worker talking to a patient in the home. The health care worker is wearing a respirator.]

Slide 106: Adverse Reactions to TB Drugs (1)

- [IMAGE: Please reference Table 4.4 Common Adverse Reactions to TB Drugs, in Module 4, pg. 33 (pdf) www.cdc.gov/tb/education/ssmodules/pdfs/tb_selfstudymodules_2015_module04.pdf]

Slide 107: Adverse Reactions to TB Drugs (2)

- [IMAGE: Please reference Table 4.4 Common Adverse Reactions to TB Drugs, in Module 4, pg. 33 (pdf) www.cdc.gov/tb/education/ssmodules/pdfs/tb_selfstudymodules_2015_module04.pdf]

Slide 108: Adverse Reactions to TB Drugs (3)

- [IMAGE: Please reference Table 4.4 Common Adverse Reactions to TB Drugs, in Module 4, pg. 33 (pdf) www.cdc.gov/tb/education/ssmodules/pdfs/tb_selfstudymodules_2015_module04.pdf]

Slide 109: TB Treatment and Monitoring Plan: Study Question 4.20

- What should be included in each patient's treatment plan?
 - Description of treatment regimen
 - Methods of monitoring for adverse reactions
 - Methods of assessing and ensuring adherence to the treatment

- Methods for evaluating treatment response

Slide 110: Adverse Reactions to TB Drugs: Study Question 4.21

- Name the drug or drugs that may cause each of the following symptoms or adverse reaction.
 - Nervous system damage:
 - INH
 - Hepatitis:
 - INH, PZA, RIF
 - Eye damage:
 - EMB
 - Orange discoloration of the urine:
 - RIF

Slide 111: TB Treatment Monitoring: Study Question 4.22

- How often should patients be monitored for adverse reactions to TB drugs?
 - All patients should be seen at least monthly during treatment and evaluated for possible adverse reactions.
 - Also, DOT providers should ask about any adverse reactions.

Slide 112: (Title Slide.) Treatment of TB Disease: Adherence and Evaluating Patients' Response to Treatment

Slide 113: Adherence to TB Treatment (1)

- Most effective strategy to encourage adherence to treatment is DOT
 - Should be considered for ALL patients
 - Should be used for all children and adolescents
 - Should be done at a time and place that is convenient for patients
- **[IMAGE: Health care worker administering DOT to a patient.]**

Slide 114: Adherence to TB Treatment (2)

- Incentives and enablers can be used to improve patient adherence
 - Incentives are rewards given to patient, e.g., gift cards
 - Enablers help patient receive treatment, e.g., bus tokens

Slide 115: Adherence to TB Treatment (3)

- Patients should be educated about TB disease and treatment
 - Cause of TB, transmission, diagnosis, and treatment plan
 - How and when to take medication
- **[IMAGE: Health care worker talking to a patient.]**

Slide 116: Monitoring Patients' Adherence to Therapy

- Patients not receiving DOT should be monitored for adherence to treatment:
 - Check if patient is reporting to clinic as scheduled
 - Ask about adherence
 - Ask patient to bring medications to clinic and count number of pills taken
 - Use urine tests to detect medication in urine
 - Assess patient's clinical response to treatment

Slide 117: Evaluating Patients' Response to Treatment (1)

- Three methods to determine whether a patient is responding to treatment:
 1. Check to see if patient has TB symptoms (clinical evaluation)
 2. Conduct bacteriologic examination of sputum or other specimens
 3. Use chest x-rays to monitor patient's response to treatment

Slide 118: Evaluating Patients' Response to Treatment (2)

- 1. Check to see if patient has TB symptoms (clinical evaluation)
 - TB symptoms should gradually improve and go away after starting treatment
 - Patients whose symptoms do not improve during the first 2 months of treatment, or whose symptoms worsen after initial improvement, should be reevaluated

Slide 119: Evaluating Patients' Response to Treatment (3)

- 2. Conduct bacteriologic examination of sputum or other specimens
 - Specimens should be examined every month until culture results have converted from positive to negative
 - Any patient whose culture results have not become negative after 2 months of treatment, or whose results become positive after being negative, should be reevaluated

Slide 120: Evaluating Patients' Response to Treatment (4)

- 3. Use chest x-rays to monitor patient's response to treatment
 - Repeated x-rays are not as helpful as monthly bacteriologic and clinical evaluations
 - Chest x-rays taken at end of treatment can be compared to any follow-up x-rays

Slide 121: Evaluating Patients' Response to Treatment (5)

- TST or IGRA cannot be used to determine whether the patient is responding to treatment
- Treatment completion is defined by number of doses the patient takes within a specific time frame
- Length of treatment depends on drugs used, drug susceptibility test results, and the patient's response to therapy

Slide 122: Reevaluating Patients Who Do Not Respond to Treatment (1)

- Reevaluating the patient means
 - Obtaining a new specimen for TB culture, and (if positive) drug susceptibility testing
 - Assessing whether the patient has taken medication as prescribed
 - Reviewing symptoms
 - Performing a clinical examination
 - Repeating chest x-rays

Slide 123: Reevaluating Patients Who Do Not Respond to Treatment (2)

- Patients should be reevaluated if:
 - Symptoms do not improve in first 2 months of therapy
 - Symptoms worsen after improving initially
 - Culture results have not become negative after 2 months of treatment
 - Culture results become positive after being negative
 - Chest x-rays show worsening

Slide 124: Adherence to Therapy: Study Question 4.23

- Name 4 ways clinicians can assess whether a patient is adhering to treatment.
 - Check whether patient is reporting to clinic as scheduled

- Ask patient to bring medications to each clinic visit and count the number of pills
- Use urine tests to detect medication
- Assess patient's clinical response to therapy

Slide 125: Adherence to Therapy: Study Question 4.24

- What is the best way to ensure that a patient adheres to treatment?
 - Directly observed therapy (DOT)

Slide 126: Response to Treatment: Study Question 4.25

- How can clinicians determine whether a patient is responding to treatment?
 - Clinical evaluations
 - Bacteriologic evaluations
 - Chest x-rays

Slide 127: Reevaluating the Patient: Study Question 4.26

- Under what circumstances should patients be reevaluated?
 - Symptoms do not improve during first 2 months of therapy
 - Symptoms worsen after improving initially
 - Culture results have not become negative after 2 months of treatment
 - Culture results become positive after being negative
 - Chest x-rays show worsening

Slide 128: Reevaluating the Patient: Study Question 4.27

- What does reevaluating the patient mean?
 - Reevaluating the patient means obtaining a new specimen for TB culture, and (if positive) drug susceptibility testing, assessing whether the patient has been taking medication as prescribed, reviewing symptoms, performing a clinical evaluation, and repeating chest x-rays.

Slide 129: (Title Slide.) Treatment of TB Disease: Role of Public Health Workers

Slide 130: Role of Public Health Workers (1)

- Successful TB treatment is the responsibility of medical providers and HCWs, not the patient
- Case management can be used to ensure that patients complete TB treatment
- A health department employee is assigned responsibility for the management of specific patients

Slide 131: Role of Public Health Workers (2)

- Provide DOT
- Help monitor patients' response to treatment
- Educate patients and families about TB
- Locate patients who have missed DOT visits or clinic appointments
- Act as interpreters, arrange and provide transportation for patients, and refer patients to other social services
- Work with private physicians to make sure TB patients complete an adequate regimen

Slide 132: Role of Public Health Workers: Study Question 4.28

- What is the goal of case management?
 - To provide patient-centered care for completion of treatment and to ensure all public health activities related to stopping TB transmission are completed.

Slide 133: Role of Public Health Workers: Study Question 4.29

- What should a public health worker do if he or she notices that a patient has symptoms of a serious adverse reaction?
 - Instruct patient to stop taking medication
 - Report situation to clinician and arrange for a medical evaluation right away
 - Note symptoms on patient's form

Slide 134: (Title Slide.) Case Studies

Slide 135: Module 4: Case Study 4.1 (1)

- You are sent to visit the home of a TB patient who was admitted to the hospital last week and diagnosed with infectious TB disease. Living in the home are his wife and his 1-year-old daughter. Neither one has symptoms of TB disease. You give them both a TST and return 2 days later to read the results. You find that the wife has 14 mm of induration, but the daughter has no induration.

Slide 136: Module 4: Case Study 4.1 (2)

- Should either one receive further evaluation for LTBI or TB disease?
 - Yes, both should receive further evaluation for LTBI or TB disease.

Slide 137: Module 4: Case Study 4.1 (3)

- Should either one start LTBI treatment? Explain.
 - Yes, both should start LTBI treatment. The wife is a contact of someone with infectious TB disease, and she has a positive TST. Therefore, after receiving a medical evaluation (and TB disease is ruled out), she should complete an entire course of LTBI treatment, regardless of her age.

Slide 138: Module 4: Case Study 4.1 (4)

- Should either one start LTBI treatment? Explain. (cont.)
 - The daughter has a negative TST, but only one week has passed since her last TB exposure. It is possible that not enough time has passed for her to be able to react to the TST.
 - Since it is currently impossible to tell whether she has TB infection and because she may develop TB disease very quickly after infection, she should start LTBI treatment now and be retested 8 to 10 weeks after last exposure to TB. If negative upon retest, she may stop taking medicine. If positive, she should complete the entire course of LTBI treatment (9 months for children).

Slide 139: Module 4: Case Study 4.2 (1)

- A 65-year-old man is prescribed LTBI treatment with INH because he is a contact of a person with infectious TB disease and he has an induration of 20 mm to the TST. His baseline liver function tests are normal, but he drinks a six-pack of beer every day.

Slide 140: Module 4: Case Study 4.2 (2)

- What kind of monitoring is necessary for this patient while he is taking INH?
 - Although his liver function tests are normal, he is at high risk of INH-associated hepatitis because he is older and he abuses alcohol.

- He should be educated about the symptoms of adverse reactions to INH and instructed to seek medical attention immediately if these symptoms occur.
- He should be seen by a clinician monthly to ask about his symptoms, examine him for signs of adverse reactions, and consider performing liver function tests.

Slide 141: Module 4: Case Study 4.3 (1)

- An 18-month-old girl is admitted to the hospital because of meningitis. Doctors discover that her grandmother had pulmonary TB disease and was treated with a 6-month regimen. The medical evaluation of the child confirms the diagnosis of TB meningitis.

Slide 142: Module 4: Case Study 4.3 (2)

- How long should the child be treated?
 - The child should be treated for 9 to 12 months because she has TB meningitis.

Slide 143: Module 4: Case Study 4.4 (1)

- You are assigned to deliver medications to TB patients as part of the DOT program where you work. When you visit Mr. Jackson's house, you ask him how he is feeling. He tells you that he was up all night vomiting.

Slide 144: Module 4: Case Study 4.4 (2)

- What are the possible causes? What should you do?
 - His vomiting may be a symptom of hepatitis (caused by INH, RIF, and PZA) or of stomach upset due to PZA. Mr. Jackson should be advised to stop his medication, and the situation should be reported to the clinician immediately. Mr. Jackson should be given a medical evaluation right away.

Slide 145: Module 4: Case Study 4.5 (1)

- Ms. Young, a patient who started treatment for TB disease last week, calls the TB clinic to complain that her urine has changed to an odd color.

Slide 146: Module 4: Case Study 4.5 (2)

- Name 2 possible causes, and explain how each would affect the color of urine.
 - One possible cause is the discoloration of body fluids, a common side effect of RIF. This would cause Ms. Young's urine to turn orange. This is NOT a serious condition.
 - Another possible cause is hepatitis, which can be caused by INH, RIF, or PZA. Hepatitis, a serious condition, would cause Ms. Young's urine to turn dark. If Ms. Young's urine is brown, the situation should be reported to the clinician and Ms. Young should receive a medical examination right away.

Slide 147: Module 4: Case Study 4.6 (1)

- Mr. Vigo was diagnosed with smear-positive pulmonary TB disease in January. He was treated with INH, RIF, and PZA by his private physician. He visited his physician again in March. His drug susceptibility test results were not available at the time of this appointment. Nevertheless, the physician discontinued his prescription of PZA and gave him refills of INH and RIF. Mr. Vigo visited his physician again in April. He had a persistent cough, and his sputum smear was found to be positive.

Slide 148: Module 4: Case Study 4.6 (2)

- What should be done next?

- Mr. Vigo's persistent cough and positive sputum smear indicate that he is not responding to therapy. The most likely explanations are:
 - He is not taking his medications as prescribed,
 - The regimen he has been prescribed is not adequate to treat his TB and he may have drug-resistant TB, or
 - A combination of the two factors listed above.
- The initial drug susceptibility test results should be located, and susceptibility tests should be repeated on a recent sputum specimen. In addition, his adherence should be evaluated, and he should be given DOT if possible.

Slide 149: Module 4: Case Study 4.7 (1)

- Ms. DeVonne began treatment for pulmonary TB disease 2 months ago, at the beginning of September. You have been supervising her DOT. During the first few weeks of therapy, you noticed that Ms. DeVonne's symptoms were improving a little. However, at a visit in October, you see that Ms. DeVonne is coughing up blood, and she tells you that she feels like she has a fever.

Slide 150: Module 4: Case Study 4.7 (2)

- What should you do?
 - You should report her symptoms to the clinician and arrange for her to receive a medical evaluation right away. Also, you should note her symptoms on her record.
 - Symptoms becoming worse after improving initially indicates that she is not responding to therapy. Because she is receiving DOT, she is probably taking her medications as prescribed. Therefore, the most likely explanation is that she has drug-resistant TB.
 - Ms. DeVonne's initial drug susceptibility test results should be located, and drug susceptibility tests should be repeated on a recent sputum specimen.