

IV. Diagnosis and Treatment of TB Disease in HIV-Negative Individuals

A. Diagnosis

Individuals with suspected TB disease should receive a medical evaluation that includes:

1. Medical and social history (e.g., the TB Epidemiological Record – DHHS 1030)
 - recent exposure - exposure within the past 2 years
 - signs and symptoms of TB disease - unexplained productive cough greater than 3 weeks of duration, anorexia, unexplained weight loss, fever, night sweats, hemoptysis
 - previous infection - if individual has taken adequate preventive therapy, TB disease is less likely
 - previous disease - if individual has taken inadequate regimen or compliance was poor, TB disease is likely to reoccur
 - risk factors - evaluate risk factors for developing disease (see Chapter II)
 - HIV infection - individuals co-infected with HIV and TB infection have a 7-10% per year risk of developing TB disease; provide HIV counseling and testing for everyone regardless of age (see Chapter V for the diagnosis and treatment of TB in HIV positive persons)
 - possible pregnancy - refer for pregnancy testing if indicated
2. TST
 - obtain documented TST mm reading **or** administer TST and record mm reading; TST is recommended but not required if the individual is known to be M. tuberculosis culture positive.
 - a positive TST supports the diagnosis of TB disease, but a negative TST does not exclude the possibility of TB disease
3. Chest x-ray
 - a posterior-anterior view of the chest is the standard radiograph for adults
 - children < 5 years of age need a posterior-anterior view and a lateral view chest x-ray
 - TB disease usually occurs in the apical and posterior segments of the upper lobe or in the superior segments of the lower lobe
 - individuals suspected of having TB disease **at any site** should have a chest x-ray and sputum smear/culture (if able to provide specimens) to rule out pulmonary involvement
4. Bacteriology
 - an early morning sputum specimen should be obtained on three consecutive days
 - all initial specimens from any source should have cultures performed
 - drug susceptibility testing should be done on all initial isolates
5. Diagnostics for suspected TB in children
 - consultation with a pediatric infectious diseases specialist is indicated when TB in a child is suspected; call your TB Nurse Consultant for assistance in making this contact
 - if the source case is unknown or the isolate is not available from the source case, obtain specimens from the child via gastric aspirate (see Chapter IX for

procedure), BAL, sputum collection or tissue biopsy if extrapulmonary disease is suspected

- if the source case is known, obtain the susceptibility test results to assure effective treatment
- if resistance is suspected in the source case or child, obtain specimens from the child for mycobacteriology
- consider an LP to rule out meningeal tuberculosis for any child <4 years old with TB; an LP is strongly recommended in children <2 years of age with suspected TB even in the absence of neurological symptoms
- any child with suspected TB and neurological symptoms should undergo prompt evaluation by a physician, preferably a pediatric infectious disease physician, an LP and an MRI with contrast

B. Treatment

1. Standards of TB Disease Management

- a. patients treated for pulmonary or extrapulmonary TB should be examined by a physician, physician's assistant or nurse practitioner:
 - within the first four weeks after presumptive or confirmed TB diagnosis
 - any time during treatment if there are signs or symptoms of significant drug toxicity
 - any time there is an indication that the patient is not responding to therapy
 - during the final month of therapy.

The exam should focus on signs and symptoms of pulmonary and extrapulmonary disease at baseline, and resolution of such findings at the end of therapy

- b. suspects of any age should have an HIV test. This information is essential to ensure adequate and appropriate treatment
- c. isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), plus ethambutol (EMB) is the standard initial four drug regimen for all HIV-negative non-pregnant individuals
- d. prior to initiating any TB therapy, review all medications the individual is taking and assess for potential drug interactions
- e. **any variation (drugs, dosage, or length of treatment) from the NC recommended regimens is to be discussed with the attending physician and the TB Nurse Consultant or the TB Control Program physician**
- f. all TB drug dosages should be calculated according to mg/kg body weight and rounded up to the next available dose supplied by the manufacturer, not to exceed maximum safe dosage for each drug; (**see dosage table later in this chapter**)

- g. adjust weight-based dosage as weight changes; young children/infants < 4 years old should be weighed monthly
- h. all tuberculosis medications should always be administered at the same time (no split doses and all TB drugs simultaneously)
- i. **directly observed therapy (DOT) is the standard of care for the management of TB disease and is required by law (10A NCAC 41 A .0205 (e))**
- j. never add a single drug to a failing regimen
- k. every patient must be assessed at least monthly for adverse reactions and the findings documented (DHHS 2810)
- l. if response is slow or sub-optimal (failure to convert sputum cultures at the end of 10 - 12 weeks of treatment and/or lack of improvement in initial symptoms), the individual should be evaluated for adherence, drug absorption, and drug resistance; treatment may need to be prolonged
- m. the standard length of treatment for uncomplicated pan-sensitive TB is a minimum of 6 months (26 wk) to include at least 4 months of treatment following sputum culture conversion
- n. **if it is necessary to use 2nd line TB drugs during treatment, the expertise of the TB Control Program physicians should be utilized**
- o. conversion is defined as "the first complete set of 3 negative cultures obtained in a series" *at least 7 days after a positive culture was obtained*; if subsequent cultures are found to be positive, this negates the conversion.
- p. if an individual is unable to produce sputum** and the attempt to collect a specimen is made under nursing supervision with clear documentation of the effort in the record, this may be considered a "clinical" conversion.

An attempt to collect an induced sputum by nebulizer should be made if a natural sputum specimen cannot be obtained (see Chapter IX for procedure**)
- q. TB medications in institutional/congregate settings should be administered daily by direct observation whenever treating disease
- r. All suspected or confirmed TB cases must be reported to the regional TB Nurse Consultant using the North Carolina Electronic Disease Surveillance System (NCEDSS) within 7 days of the patient being identified as a suspect
- s. see variations in the length of treatment under specific regimens found in the remainder of this chapter
- t. The physician should review and sign all lab results.

2. Standard Regimen for HIV-negative Adults ≥ 15 yr. with Pulmonary TB

- a. the **initial phase** (8 weeks) is intended to rapidly reduce the number of tubercle bacilli in the body. This phase consists of four-drug therapy:
- INH, RIF, PZA, EMB, daily DOT for 2 weeks (14 doses, 10 of which must be directly observed), then twice-weekly DOT (**dose must be increased for intermittent therapy**) for 6 weeks (12 twice-weekly doses)
 - **if PZA is not included in the initial regimen, the first 8 weeks of treatment must be administered by daily DOT**
 - if PZA is not included in the regimen within the first 2 weeks of treatment or PZA is contraindicated, a minimum of **nine months** of INH and RIF is required. (2 months of PZA at the beginning of treatment is required for a 6 month or short course regimen to be effective)
 - discontinue PZA after 8 weeks if the organism is fully susceptible to INH and RIF and the patient is tolerating both drugs **-or-** after 8 weeks if the initial cultures were negative and the individual is clinically improving
 - discontinue EMB when drug susceptibility testing on the initial positive culture indicates that the organism is fully susceptible to INH, RIF and PZA and these drugs will remain in the regimen **-or-** at 8 weeks when an individual with negative cultures is determined to be improving clinically and tolerating the remaining drugs
- b. the **continuation phase** (18 weeks) is intended to eliminate the smaller number of organisms that persist. If treatment is not continued long enough, some bacilli may survive and cause TB disease later. This phase consists of INH and RIF twice-weekly DOT for 18 weeks (36 twice-weekly doses).
- c. for patients who are initially sputum culture positive, sputum specimens must be collected every 2 weeks after treatment is initiated until a series of 3 cultures has converted to negative
- d. if the patient has a cavity on initial x-ray **and** fails to convert 3 sputum specimens to negative within the first 2 months of treatment (based on the collection date), treatment must be extended for a total of 9 months (**continuation phase of 31 weeks OR 62 twice-weekly doses**)

3. Regimen for HIV-negative Pregnant Women

- a. INH, RIF, and EMB daily for 8 weeks DOT (initial phase) followed by 31 weeks of INH and RIF (if fully susceptible) twice weekly DOT (continuation phase). (56 daily doses plus 62 twice-weekly doses)
- the first 8 weeks of medicine must be administered on a daily basis since PZA is not routinely used during pregnancy,
 - discontinue EMB when initial culture results confirm fully susceptible organisms - or at 8 weeks if the initial cultures were negative **and** the individual is clinically improving
- b. **PZA** is not routinely used in the U.S. in HIV-negative pregnant women because its effect on the fetus is unknown

- c. **streptomycin** should not be used when treating pregnant women because it interferes with the development of the ear and may cause congenital deafness
 - d. vitamin B6 should be given due to the risk for peripheral neuropathy in pregnancy
 - e. INH, RIF and EMB all cross the placenta but these drugs have not been demonstrated to have teratogenic effects on the fetus
 - f. small concentrations of TB medications in breast milk do not produce toxicity in the nursing newborn; therefore, breast-feeding should not be discouraged. (see Chap. III regarding breast-feeding and B₆)
4. Regimen for HIV-negative Infants and Children (<15 yr.)
- a. refer to special diagnostics on page IV-1 of this chapter when TB in a child is suspected and obtain consultation from a pediatric infectious disease specialist
 - b. treatment of suspected central nervous system (CNS) TB should include steroids in addition to the standard TB drugs
 - c. **initial phase** (8 weeks) is intended to rapidly reduce the number of tubercle bacilli in the body. This phase consists of
 - INH, RIF, PZA, and EMB, daily DOT for 2 weeks (14 doses, 10 of which must be directly observed), then twice-weekly DOT (**increase dose for intermittent therapy**) for 6 weeks (12 twice-weekly doses)
 - use EMB with caution for children who are unable to be vision-tested
 - INH dosing for children can be calculated as follows

Tablets:	To calculate number of kg, divide individual's weight by 2.2. (1 kg = 2.2 lbs.). Multiply weight in kg by recommended mg per kg based on daily or twice weekly regimen.
INH syrup:	To calculate number of kg, divide individual's weight by 2.2. (1 kg = 2.2 lbs.). Multiply weight in kg by recommended mg per kg based on daily or twice weekly regimen. INH syrup concentration is 10 mg/cc.
 - d. **continuation phase** (18 weeks) is intended to eliminate the smaller number of organisms that persist. If treatment is not continued long enough, some bacilli may survive and cause TB disease later. This phase consists of INH and RIF twice weekly DOT for 18 weeks (36 twice-weekly doses)
 - discontinue EMB when initial cultures results confirm fully susceptible organisms or at 8 weeks if the initial culture results were negative **and** the child is clinically improving
 - discontinue PZA after the initial 8 weeks if culture results confirm fully susceptible organisms - or - if the initial culture results were negative **and** the child is clinically improving

- e. *infants and children with meningeal, bone/joint or miliary TB should receive a minimum of 9-12 months of treatment*
 - f. if PZA is not included in the first 8 weeks, the initial phase of treatment must be administered by daily DOT and the regimen must be extended to 9 months.
 - g. infants and children should be weighed monthly and drug dosages adjusted accordingly
 - h. children weighing more than 40 kg should be dosed as adults
 - i. chest x-rays of children with hilar adenopathy may not become normal for 2-3 years after treatment. A normal chest x-ray is not required to consider treatment complete.
5. Regimen for HIV-negative Non-Pregnant Adults with Smear and Culture Negative Pulmonary TB
- a. treatment consists of INH, RIF, PZA, and EMB for 8 weeks. (14 daily doses, 10 of which must be directly observed, plus 12 twice weekly doses) At the completion of 8 weeks of treatment, discontinue PZA and EMB and continue with INH and RIF for a total of 16 weeks of treatment (16 additional twice weekly doses) **(if HIV-positive, treat for a total of 26 weeks; see Chapter V for further information)**
 - b. obtain a chest film after 2 months of treatment. If there is no improvement on x-ray, consult the physician regarding a possible change in the diagnosis.
 - c. if the source case is known to have drug resistant TB, refer to the regimens for resistant TB in this chapter
6. Regimen for HIV-negative Adults with Extrapulmonary Tuberculosis
- Individuals with TB disease at any site should have a chest x-ray and sputum specimens for smear/culture (if able to produce sputum) done during the diagnostic phase to rule out pulmonary involvement
- a. extra-pulmonary TB can be treated with the same drug regimens and for the same length of time as pulmonary TB (standard 6 month regimen - 26 wks) with the following exceptions:
 - meningeal/CNS TB should be treated for 9-12 months based on response to treatment
 - bone/joint TB should be treated for 9-12 months based on response to treatment
 - If there are questions regarding a prescribed treatment regimen, please consult with the NC TB Control Program
 - b. corticosteroids can be beneficial in preventing cardiac constrictions from TB pericarditis and in decreasing neurologic sequelae of all stages of TB meningitis, particularly if administered early in the course of disease

7. Rifapentine (RPT) Option for Treating HIV-negative Adults \geq 18 years old
- a. once weekly INH and RPT may be used in selected patients during the continuation phase of treatment. The following guidelines were developed in 2003 following the publication of the new American Thoracic Society (ATS) treatment statement.
 - b. the patient must meet all of the following "inclusion" criteria for rifapentine to be a treatment option:
 - culture confirmed pulmonary TB
 - completion of the initial phase of treatment (8 weeks) with INH, RIF, PZA & EMB (EMB may have been discontinued if the organism was fully susceptible)
 - TB fully susceptible to INH, RIF, PZA & EMB
 - non-cavitary chest films
 - negative sputum smears at 8 weeks or earlier
 - evidence of clinical improvement
 - documentation of a negative HIV test result within the past six months; persons with current risk factors for HIV may need to be re-tested
 - age \geq 18 years
 - tolerant of rifampin
 - fully compliant with current treatment
 - signed TB Treatment Agreement (**see sample agreement later in this chapter**)
 - TB Nurse Consultant approval obtained
 - c. if the patient has any of the following "exclusion" criteria, rifapentine is not an option:
 - bone/joint, meningeal, or silicotuberculosis (in addition to pulmonary TB)
 - cavitary chest films
 - positive sputum smears at 8 weeks
 - HIV seropositive
 - lack of documented HIV test result within the past six months
 - age $<$ 18 years
 - pregnant or breastfeeding
 - d. treatment regimen dosages
 - RPT 600 mg once weekly x 18 weeks (10 mg/kg of body weight with a maximum dose of 600 mg.)
 - INH 900 mg once weekly x 18 weeks (15 mg/kg of body weight with a maximum dose of 900 mg)
 - B₆ 50 mg once weekly x 18 weeks (**Give only if indicated in the guidelines found later in this chapter**)
 - e. additional treatment criteria
 - all doses must be directly observed
 - adherence with this regimen is essential; any missed doses must be made up
 - doses must be at least 72 hours apart

- the patient may be switched to rifapentine at any point in the continuation phase of treatment if the criteria for this option are met
- if the patient's sputum cultures do not convert to negative in 8 weeks, the continuation phase must be extended an additional 12 weeks, thereby extending the total length of treatment from 6 to 9 months (39 weeks)
- if the patient misses 2 weekly doses, he/she should be switched back to a standard INH/RIF twice weekly DOT regimen

8. Treatment of *M. bovis* Including BCG Strain

- if *M. bovis* is isolated from urine specimens following intravesical BCG treatment, treatment for TB disease will depend on the extent of clinical manifestations of TB disease
- if *M. bovis* is isolated from pulmonary specimens following intravesical BCG treatment, the patient should receive treatment for tuberculosis disease
- if you receive a positive *M. tuberculosis complex* culture report on an individual who has been treated with BCG for bladder cancer, notify your Nurse Consultant
- M. bovis* is always resistant to PZA
- use INH and RIF for the initial regimen and treat for 9 months (39 weeks) using daily administration during the first 8 weeks

Remember that *M. bovis* is one of the organisms found in mycobacterium tuberculosis complex (see Chapter IX, Laboratory Services). If drug susceptibility testing shows mono-resistance to PZA, the disease is due to *M. bovis* and the state lab will run further studies to determine if it is the BCG strain.

C. Drug Resistant TB

- Patients who are resistant to TB drugs will need an alternative regimen. The alternative regimen should be discussed with a state TB Medical Consultant on a case-by-case basis
- Primary resistance occurs when resistant tubercle bacilli are isolated before any TB drugs are administered. Risk factors for primary resistance are:
 - exposure to a TB patient who has drug-resistant TB disease
 - being from a country with a high prevalence of drug resistance
 - residing in a population with $\geq 4\%$ resistance to INH
- Acquired resistance occurs when resistant tubercle bacilli are isolated during treatment or isolated from those who have been treated in the past. Risk factors for acquired resistance are:
 - individuals who do not follow their prescribed treatment schedule

- b. inadequate or inappropriate drug regimen
 - c. malabsorption (can lead to sub-therapeutic serum drug levels)
4. Regimens for INH Resistance or Intolerance (**Consult with a State TB Medical Consultant**)
- a. individuals on an initial regimen of INH, RIF, PZA, and EMB
 - discontinue INH; continue to treat with RIF, PZA, and EMB for a total of 6 months (26 weeks)
 - b. individuals on an initial regimen of INH, RIF, and EMB (no PZA)
 - discontinue INH; continue to treat with RIF and EMB
 - the initial phase (the first 8 weeks) must be administered by daily DOT
 - Treat for a minimum of 12 months
 - c. individuals on initial regimen of INH and RIF
 - repeat susceptibility studies,
 - discontinue INH and continue RIF,
 - add PZA and EMB to the regimen if susceptible to these two drugs and then treat for 6 months (26 weeks) with the 3 drugs
5. Regimen for RIF Resistance or Intolerance (**Consult with a State TB Medical Consultant**)
- a. individuals on initial regimen of INH, RIF, PZA, and EMB
 - discontinue RIF
 - continue to treat with INH, PZA and EMB daily during the initial phase (the first 8 weeks)
 - after the initial phase continue INH and EMB daily or intermittently
 - treat for a total of 18 months (78 weeks)
6. Regimen for PZA Resistance or Intolerance (**Consult with a State TB Medical Consultant**)
- a. an "M.tuberculosis complex" isolate that is PZA resistant is likely to be M.bovis which is always PZA resistant. M.bovis can be acquired through unpasteurized milk or cheese, and, if the site of disease is pulmonary, can be spread to others
 - b. individuals on an initial regimen of INH, RIF, PZA and EMB
 - discontinue PZA and EMB if sensitive to RIF and INH
 - treat with INH and RIF for 9 months (39 weeks)
 - The initial phase (the first 8 weeks) must be administered by daily DOT
7. Multi-Drug Resistant TB (MDR-TB) (**Consult with a State TB Medical Consultant**)
- a. MDR-TB is resistant to both INH and RIF and may also be resistant to other first or second line drugs

- b. treatment must be individualized and prolonged based on medication history and susceptibility studies
- c. give at least 3 medications to which the organism is susceptible
- d. the regimen should continue until sputum conversion is documented, followed by at least 12 months of treatment
- e. only daily therapy is used in the treatment of MDR-TB
- f. **the NC TB Control Program should be consulted regarding the treatment regimen whenever treating an MDR-TB case**

D. Pyridoxine (B₆)

1. Peripheral neuropathy is associated with INH but is uncommon at dosages of 5 mg/kg of body weight
2. Patients with the following conditions in which neuropathy is common should receive B₆ 25 mg. daily or 50 mg twice or thrice weekly:
 - diabetes mellitus
 - average alcohol use of >3 drinks per day
 - malnutrition
 - HIV infection
 - pregnancy
 - seizure disorder
3. Pyridoxine (B₆) is recommended for exclusively breastfed infants and for children and adolescents on milk and meat and deficient diets; children with nutritional deficiencies, including all symptomatic HIV-infected children.
 - Dosage for infants and children (contact physician for order): 1 mg/kg body weight (maximum 25mg daily)
4. Individuals that develop peripheral neuropathy while taking daily B₆ should have their B₆ dose doubled. If neuropathy is not resolved within 2 weeks, consult the physician.
5. Individuals on dialysis should be given B₆ 50mg on the same schedule as INH

E. Dosing for Adults with Reduced Renal Function (creatinine clearance <30ml/min) on Hemodialysis¹

1. Medications should be given after hemodialysis on the day of dialysis (dialysis is normally done 3 times a week)
 - a. monitoring of serum drug concentrations should be considered to ensure adequate absorption and to assist in avoiding toxicity
 - b. ethambutol is difficult to manage in renal insufficiency and therefore is used less often, usually only when resistance is an issue

- c. there is no clinical evidence for using 250 mg of cycloserine daily; there should be careful monitoring for evidence of neurotoxicity

Isoniazid	No change	300 mg daily or 900 mg twice or thrice weekly
Rifampin	No change	600 mg daily or twice or thrice weekly
Pyrazinamide		25-30 mg/kg twice or thrice weekly (not daily)
Ethambutol		15-25 mg/kg twice or thrice weekly (not daily)
Levofloxacin		750-1000 mg twice or thrice weekly (not daily)
Cycloserine		250 mg daily or 500 mg twice or thrice weekly
Ethionamide	No change	250-500 mg daily
PAS	No change	4 Gm, twice daily
Streptomycin		12-15 mg/kg twice or thrice weekly (not daily)
Capriomycin		12-15 mg/kg twice or thrice weekly (not daily)
Kanamycin		12-15 mg/kg twice or thrice weekly (not daily)
Amikacin		12-15 mg/kg twice or thrice weekly (not daily)

¹ Centers for Disease Control and Prevention. Treatment of Tuberculosis. American Thoracic Society, CDC, and Infectious Diseases Society of America. MMWR 2003; 52 (No. RR-11): 63-64.

F. Directly Observed Therapy

1. **Directly Observed Therapy (DOT) is the standard of care for the management of TB disease and is required by law (10A NCAC 41 A .0205 (e))**
2. Directly Observed Therapy (DOT) is the documented actual observation of medication ingestion by a health care worker (HCW). This specifically excludes family members and significant others.
3. Document each DOT dose on the back of the Tuberculosis Drug Record (DHHS 1391)
 - a. when DOT is delegated to a health care worker outside the health department, the TB nurse retains ultimate responsibility for documenting the monthly patient assessment (regardless of who observed the medication ingestion) and for patient management
 - b. document the observer's understanding and willingness to:
 - assume responsibility for actual observation of ingestion
 - document ingestion of TB drugs
 - report to PHN any patient complaints
 - notify PHN immediately when dose(s) are missed
 - request relief from DOT responsibility if does not wish to continue
4. Daily DOT must be administered Monday through Friday. Unit doses may be self-administered on weekends; Five DOT doses are considered a DOT week.
5. Twice weekly DOT requires a physician's order to increase the dosage and is administered on a Monday/Thursday or Tuesday/Friday schedule.

6. Twice and thrice weekly dosages should not be given to the patient to self administer. If the patient must self administer, such as, during a vacation, daily dosing should be given to the patient to self administer.
7. Twice weekly DOT scheduling should be adjusted for holidays so that both doses can be given by DOT that week; it is permissible to give both twice weekly doses within 48 hours if holidays require doing so.
8. In order to insure that all doses are administered by DOT, please make up any self-administered doses (except weekends) with a DOT dose; this will allow for 100% DOT when reporting to the TB Control Program using the CDC Follow Up 2 form and will ensure adequate treatment.

G. Monitoring

1. Baseline Evaluation
 - a. the TB Nurse needs to visit the patient either in the hospital or in the home as soon as possible after notification to establish a working relationship
 - b. obtain medical history using the TB Epidemiological (EPI) Record (DHHS 1030), including the patient's informed consent
 - c. complete a baseline evaluation using the Tuberculosis Flow Sheet (DHHS 2810)
 - d. obtain a signed TB Treatment Agreement (**see sample agreement later in this chapter**). Include the following in the document:
 - treatment regimen and frequency
 - required monitoring e.g. x-rays, sputum, lab work, appointments
 - other requirements pertinent to the situation
 - e. if infectious, advise the patient to remain at home, exclude outside visitors and wear a mask to medical appointments until becomes non-infectious as determined by the health department
 - f. collect supervised sputum regardless of prior pulmonary or pleural specimens obtained elsewhere. Provide individual with two additional containers for collection of consecutive early morning specimens to be sent to the State Laboratory. (**refer to Chapter IX for procedure**)
 - g. have patient identify persons at risk for exposure and possible infection and prepare a list of contacts for tuberculin skin testing
 - h. obtain documented TST mm reading **or** administer TST and record mm reading; TST is recommended but not required if the individual is known to be M. tuberculosis culture positive.
 - i. draw blood or obtain laboratory results for those ≥ 15 years old including

- hepatic function panel
 - serum creatinine
 - CBC with platelet
- j. consult physician if any baseline laboratory test is abnormal; if within normal limits, no further testing is necessary unless the patient has evidence of toxicity.
 - k. all children and adults should have HIV testing done or results documented
 - l. individuals taking Ethionamide and p-Aminosalicylic acid (PAS) should have thyroid function tests (e.g., TSH) monitored at least monthly
 - m. individuals taking Streptomycin, Amikacin, Kanamycin, and Capreomycin should have BUN and Creatinine monitored at baseline and at least monthly
 - n. individuals taking Capreomycin should have potassium and magnesium monitored at baseline and monthly
 - o. perform baseline visual acuity (Snellen) and color perception testing (red/green- Ishihara test) on individuals to be treated with ethambutol
 - p. perform baseline hearing/ataxia testing on individuals to be treated with streptomycin (SM), Capreomycin, Kanamycin, and Amikacin using screening audiometry and tandem gait test (heel to toe in a straight line for 4-6 steps)
 - q. calculate and verify each prescribed medication dosage. Calculate on the lower figure in the range and round up to the next available dose supplied by the manufacturer; any dosage within the therapeutic range is acceptable.
2. Follow-up monitoring:
 - a. complete the Tuberculosis Flow Sheet (DHHS 2810) monthly
 - b. make a home visit to:
 - further identify personal and socioeconomic barriers to treatment adherence
 - re-interview to ensure all contacts have been identified
 - c. obtain a set of three consecutive early morning sputum specimens every two weeks (if diagnostic specimen was sputum), until cultures convert to negative. **Supervise the collection of one specimen in each set.**
 - d. check visual acuity (Snellen) and color perception (red/green, Ishihara test) **monthly** while individual is taking EMB. Report any changes in visual acuity or color perception to the TB physician.

- e. individuals taking Streptomycin, Amikacin, Kanamycin, and Capreomycin should have BUN and Creatinine monitored at least monthly
- f. individuals taking Capreomycin should have potassium and magnesium monitored monthly
- g. perform hearing acuity using screening audiometry and tandem gait test (heel to toe in a straight line for 4-6 steps) monthly while individual is taking SM, capreomycin or amikacin, or kanamycin. Report any changes in audiometric screening or tandem gait testing to the TB physician
- h. obtain monthly hepatic function panel for the following individuals:
 - abnormal baseline hepatic function
 - pregnant or up to 3 months postpartum
 - those with symptoms of adverse reactions
 - persons taking potentially hepatotoxic drugs
 - persons with chronic active hepatitis B or those with hepatitis C
- i. consult physician anytime hepatic function testing results are abnormal
- j. If the patient does not clinically improve and/or sputum cultures do not convert from positive to negative within 10-12 weeks:
 - arrange for patient to be evaluated by a physician or mid-level provider
 - repeat susceptibilities testing on latest positive MTB sputum culture if cultures are still positive at 10-12 weeks
 - consult with regional TB nurse consultant regarding serum drug levels. Information regarding serum drug levels may also be found in chapter IX
 - consult with the state TB medical clinician to discuss serum drug level results, appropriate dosing of TB medicines, and length of therapy
- k. review at least monthly for hepatotoxicity and other drug reactions:
 - nausea
 - vomiting
 - loss of appetite
 - dark urine (cola color)
 - yellow skin or sclera
 - malaise
 - abdominal tenderness
 - unexplained fever of 3 or more days
 - unexplained abdominal bloating
 - rash
 - pruritus
 - paresthesias of the hands or feet
 - bruising
 - flu-like symptoms
 - abnormal bleeding

- l. if the individual exhibits signs or symptoms of possible toxicity:
 - temporarily stop the medications
 - do lab work appropriate to symptoms
 - contact the prescribing physician to discuss symptoms, lab results, and any needed changes in the treatment plan
 - patients with confirmed or strongly suspected TB should not remain off all TB medications for much longer than a week. Consultation with one of the State TB physicians should be initiated if there is any question or delay in finding an acceptable treatment regimen
- m. obtain a chest x-ray after 2 months of treatment if pre-treatment culture results were negative. If no improvement on x-ray, consult physician regarding possible change in original diagnosis
- n. obtain a chest x-ray during the final 2 weeks of therapy on all individuals with pulmonary and pleural TB disease. This provides a comparison film for future reference. Length of treatment should not be based on end of treatment chest x-ray results
- o. the patient should be evaluated by the referring physician, primary care provider or health department TB physician in the final weeks of treatment.
- p. discharge the individual from service after providing education and instructions to return if symptoms occur. A record of completion of TB treatment should be given to the patient to keep as part of his personal medical record

H. TB Drug Adverse Reactions

Evaluation of all adverse reactions should include a hepatic function panel to rule out hepatotoxicity and consultation with the prescribing physician.

- 1. Rash
 - a. if the rash is minor and or manifested primarily by itching, the medical provider may treat with antihistamines which may provide symptomatic relief
 - b. if the rash is petechial, it may be due to rifampin induced thrombocytopenia. Stop TB medicines and contact TB physician. Obtain order for CBC with diff and platelets and report results to TB physician as soon as possible. If rifampin is discontinued due to thrombocytopenia notify regional nurse consultant
 - c. if there is a generalized erythematous rash, particularly if associated with fever and/or mucous membrane involvement, stop all drugs immediately and notify physician.
 - d. if patient experiences swelling of the face, throat or difficulty breathing, call 911 and activate emergency services immediately

- 2 Nausea/vomiting and other GI distress
 - a. obtain a hepatic function panel to rule out hepatotoxicity
 - b. if no hepatotoxicity is present, the provider should consider the use of an anti-nausea medicine 30 minutes before the TB medications are administered or offer TB drugs with food
3. Hepatotoxicity
 - a. if signs and symptoms of hepatotoxicity are **present**:
 - temporarily stop medications
 - draw hepatic function panel
 - contact the prescribing physician to discuss symptoms and lab results and any needed changes in the treatment plan
 - the prescribing physician should refer to the hepatotoxicity flowchart in chapter III.
 - contact the regional TB Nurse Consultant if ALT>3 times the upper limit of normal (ULN) or the bilirubin is < 2.5
 - b. if signs and symptoms of hepatotoxicity are **not present**, manage individuals according to hepatotoxicity flowchart in chapter III, pages 10-12
 - c. hepatitis due to other causes needs to be ruled out using appropriate serologies e.g., HBsAg, antiHBc-IgM, HAV IgM, HCV
 - d. Changes to a standard four drug TB regimen (INH, RIF, EMB, PZA) must be okayed by a state TB medical consultant

I. Reintroduction of TB Medication for Hepatotoxicity

1. **Stop all TB medications if lab work is abnormal and consult physician.** Patients with confirmed or strongly suspected TB should not remain off all TB medications for much longer than a week. Consultation with one of the State TB physicians should be initiated if there is any question or delay in finding an acceptable treatment regimen
2. Monitor liver enzymes until level reflects a continuing decrease before restarting any TB drugs (< 2x ULN)
3. Reintroduce drugs in the following order (see protocol below):
 - ethambutol (EMB) and rifampin (RIF)
 - isoniazid (INH)
 - pyrazinamide (PZA)
 - PZA is reintroduced only if individual has not completed the initial 8 weeks of PZA. Incremental dosing of PZA as follow: 500 mg on day 11; 1000 mg on day 12; 1500 mg on day 13; and full dose daily thereafter
 - EMB is reintroduced at a full therapeutic dose if drug susceptibilities are not yet available and the drug is needed for the initial treatment regimen.

4. Monitor liver enzyme levels weekly and evaluate results before adding another drug to the regimen
5. Because reintroduction takes approximately 3 weeks, it may be prudent to give at least 3 non-hepatotoxic TB drugs during this time, e.g., EMB, SM and a quinolone
6. Contact North Carolina Tuberculosis Control for assistance in determining the appropriate length of therapy once reintroduction of drugs is complete and therapeutic dosages are achieved

J. Suggested Flow Chart for Reintroducing TB Medications (daily administration)

Week #1:

Dose #1	EMB (full dose), RIF 600 mg
Dose #2	EMB, RIF 600 mg
Dose #3	EMB, RIF 600 mg.
Dose #4	EMB, RIF 600 mg
Dose #5	EMB, RIF 600 mg

Draw hepatic function panel

Week #2:

Dose #6	EMB, RIF 600 mg, INH 300 mg
Dose #7	EMB, RIF 600 mg, INH 300 mg
Dose #8	EMB, RIF 600 mg, INH 300 mg
Dose #9	EMB, RIF 600 mg, INH 300 mg
Dose #10	EMB, RIF 600 mg, INH 300 mg

Draw hepatic function panel

Week #3:

Dose #11	EMB, RIF 600 mg, INH 300 mg, PZA 500 mg
Dose #12	EMB, RIF 600 mg, INH 300 m, PZA 1000mg
Dose #13	EMB, RIF 600 mg, INH 300mg, PZA 1500 mg
Dose #14	EMB, RIF 600 mg, INH 300mg, PZA full dose
Dose #15	EMB, RIF 600 mg, INH 300mg, PZA full dose

Draw hepatic function panel

K. Airborne Precautions and/or Home Isolation

1. Transmission of TB is dependent upon four factors:
 - a. number and/or viability of bacilli expelled in air (index case characteristics)
 - b. susceptible host (contacts)
 - c. environment (shared air)
 - d. duration and/or frequency of exposure (time)
2. Individuals newly suspected of having pulmonary or laryngeal TB are considered infectious and should be managed using airborne precautions with no new persons exposed until the following conditions have been met:

- a. individuals who are initially sputum smear positive should be maintained in negative pressure isolation while in the hospital or restricted to their home until
 - 3 consecutive sputum specimens at least 8 hours apart are found to be smear negative for AFB,
 - they have been compliant on TB medicine to which the organism is judged to be susceptible, and
 - they show evidence of clinical improvement
 - b. individuals initially sputum smear negative should be maintained in negative pressure isolation while in the hospital until they have been compliant on tuberculosis medications to which the organism is judged to be susceptible and there is evidence of clinical improvement on treatment
 - c. individuals needing respiratory precautions may be discharged to their home regardless of sputum smear status with instructions to remain in the home, avoid exposing anyone other than already exposed household members and to avoid contact with infants and young children and immunocompromised individuals. The local health department will advise when the precautions can be lifted based on length of treatment and sputum smear status.
 - d. it is critical that a person with positive smears not be permitted to return to an institutional or congregate setting, a setting with infants and children, or a setting where immunocompromised individuals are located. An outdoor work environment may be permissible in some circumstances; this first needs to be discussed with the Nurse Consultant
 - e. persons with suspected or known active pulmonary or laryngeal TB who are initially sputum smear negative AND who will be managed at home (not in hospital) do not require respiratory isolation once they have been started on tuberculosis treatment
3. Hospitalized pediatric TB suspects and cases should be managed in accordance with specific pediatric infection control policies. Parents or guardians should be evaluated for TB disease early in the hospital stay.

"Children younger than 10 years of age with primary tuberculosis rarely are contagious because their pulmonary lesions are small (paucibacillary disease), cough is not productive, and few or no bacilli are expelled." (American Academy of Pediatrics. *Tuberculosis*. In: Pickering LK, ed. Red Book: 2006 Report of the Committee on Infectious Diseases, 27th ed. Elk Grove Village, IL: American Academy of Pediatrics, 2006: 680.

L. Reporting Cases

1. Report cases to the TB Control Program that meet the laboratory or clinical TB case definition.
 - a. laboratory confirmed cases:
 - Isolation of *M. tuberculosis* complex from a clinical specimen. The use of rapid identification techniques for *M. tuberculosis* performed on a culture from a clinical specimen, such as DNA probes and high-pressure liquid chromatography (HPLC), is acceptable under this criterion.

OR

- Demonstration of *M. tuberculosis* from a clinical specimen by nucleic acid amplification (NAA) test. NAA tests must be accompanied by cultures of mycobacterial species. However, for surveillance purposes, CDC will accept results obtained from NAA tests approved by the FDA and used according to the approved product labeling on the package insert, or a test produced and validated in accordance with applicable FDA and Clinical Laboratory Improvement Amendments (CLIA) regulations

OR

- Demonstration of acid-fast bacilli (AFB) in a clinical specimen when a culture has not been or cannot be obtained or is falsely negative or contaminated; historically this criterion has been most commonly used to diagnose TB in the postmortem setting.

b. clinical case definition. In the absence of laboratory confirmation of *M. tuberculosis* complex after a diagnostic process has been completed, persons must have **all** of the following criteria for clinical TB

- evidence of TB infection based on a positive tuberculin skin test result or positive interferon gamma release assay for *M. tuberculosis*

AND

- one of the following
 - signs and symptoms compatible with current TB disease, such as an abnormal chest radiograph or abnormal chest computerized tomography scan or other chest imaging study, or
 - clinical evidence of current disease (e.g., fever, night sweats, cough, weight loss, hemoptysis)

AND

- current treatment with two or more anti-TB medications

c. a final diagnosis should be made by the TB clinician, in conjunction with the treating physician if indicated, within 2 months of initiating therapy

d. submit the Report of Verified Case of TB (RVCT) and Follow Up 1 report to the TB Nurse Consultant for your county when drug susceptibilities are known and within 3 months of initiating treatment

2 Special Reporting Situations

a. immigrants, refugees, permanent resident aliens, border crossers, and foreign visitors

- Immigrants and refugees who are examined after arriving in the United States and diagnosed with clinically active TB requiring anti-TB medications should be counted by the locality of their current residence at the time of diagnosis regardless of citizenship status
- border crossers and permanent resident aliens who are diagnosed with TB and plan to receive anti-TB therapy from a locality in the United States for 90 days or more should be counted by the locality of current residence.

b. out-of-state or out-of area residents

- a person's TB case should be counted by the locality in which he or she resides at the time of diagnosis. TB in a person who has no address should be counted by the locality that diagnosed and is treating the TB. The TB control officer should notify the appropriate out-of-state or out-of-area TB control officer of the person's home locality to (1) determine whether the case has already been counted to avoid "double counting," and (2) agree on which TB control office should count the case if it has not yet been counted.
- c. migrants and other transients
- persons without any fixed U.S. residence are considered to be the public health responsibility of their present locality and their TB case should be reported and counted where diagnosed.
- d. federal facilities (e.g., military and veterans administration facilities)
- cases in military personnel, or dependents, or veterans should be reported and counted by the locality where the persons are residing in the United States at the time of diagnosis and initiation of treatment. However, if military personnel or dependents are discovered to have TB at a military base outside the United States but are referred elsewhere for treatment (e.g., a military base located within the United States), the TB case should be reported and counted where treated and not where the diagnosis was made.
- e. Indian health services
- TB should be reported to the local health authority (e.g., state or county) and counted where diagnosed and treatment initiated. However, for a specific group such as the Navajo Nation, which is geographically located in multiple states, health departments should discuss each case and determine which locality should count the case.
- f. correctional facilities (e.g., local, state, federal, and military)
- Persons who reside in local, state, federal, or military correctional facilities may frequently be transferred or relocated within and/or between various correctional facilities. TB in those persons should be reported to the local health authority and counted by the locality where the diagnosis was made and treatment plans were initiated.
- g. peace corps, missionaries, and other citizens residing outside the United States
- TB in persons diagnosed outside the United States should not be counted. TB in these persons should be counted by the country in which they are residing regardless of their plans to return to the United States for further work-up or treatment.
- h. if TB recurs (relapse) in an individual **and** if more than 12 months have elapsed since the individual completed treatment, the recurrence is considered a separate episode and should be counted as a new case
- i. if the case is lost to follow-up but is then located and restarted on treatment, this is not a separate episode; the RVCT Follow Up 2 form

should be updated to reflect a new Reason Therapy Stopped and Date Stopped when the person completes treatment or has another outcome.

- j. notify the state of residence or state to which a NC case is moving using the Interjurisdictional TB Notification Form (**see Chapter X for instructions and form**); a copy of the form should be placed in the patient's record.
- k. forward information regarding cases with residence in another NC county to the appropriate county for case counting
- l. Obtain assistance from the NC TB Control when making international referrals

M. HIV Reporting

TB in persons who are HIV-positive is an AIDS defining condition

Verify that a CD card and Adult HIV/AIDS Confidential Case Report (CDC 50-42A) have been sent to the HIV/STD Section for TB cases who are HIV-positive

N. Death Certificates

1. Review and investigate death certificates that list TB as a cause of death or contributing condition. Count as a TB case if confirmed and not previously reported.
2. If TB was not the cause of death, ask the physician to amend the death certificate as follows:
 - a. attending physician completes Supplemental Report of Cause of Death (**DHHS 2263**)
 - b. original DHHS 2263 is forwarded to Vital Records in Raleigh
 - c. one copy is kept at health department, and
 - d. one copy is sent to Register of Deeds in the county where the individual died

O. Patient Non-Adherence

1. Evaluate for barriers to adherence at initial patient contact. The following factors should be taken into consideration:
 - lack of social or family support
 - alcohol abuse
 - substance abuse
 - homelessness
 - history of non-adherence in other health care situations
 - mental and/or emotional instability
2. Evaluate for non-adherence during the treatment phase, such as:
 - refusing medication

- taking medication inconsistently
 - failing to keep DOT appointments
 - missing clinic appointments
3. If the patient does not abide by the TB Treatment Agreement (see sample agreement in this chapter) **or** has missed a total of 2 weeks treatment during the initial phase or 3 weeks of treatment during the continuation phase, then an Isolation Order should be issued by the Health Director
 4. The intent of the Isolation Order is to ensure that the patient has been fully informed of the legal requirements for treating disease and understands legal action can be taken if there is any non-adherence from that date forward; do not issue an Isolation Order and then fail to follow up with legal action if it becomes necessary.
 5. An Isolation Order does not have to be issued before taking out a warrant for the arrest of a health law violator.
 6. If there is reason to believe that the patient may board an airplane while infectious, contact NC TB Control with assistance is having the patient's name added to the Do Not Board list.

P. N.C. Public Health Laws and TB

See Chapter XI for complete language found in the General Statutes (G.S.) and Communicable Disease rules.

1. General Statute 130A-144
 - a. provides the authority for the local health director to investigate all cases of communicable diseases or conditions
 - b. calls for the adoption of rules that prescribe control measures for communicable diseases and conditions, and
 - c. requires that all persons comply with control measures, including submission to examinations and tests
2. General Statute 130A-145 gives quarantine and isolation authority to the State Health Director and local health directors.
3. General Statute 130A-25 states it is a misdemeanor to violate G.S. 130A-144(f) or G.S. 130-145 and specifically states that a person convicted of violating either of these General Statutes shall be sentenced for no more than two years and may not be released prior to the 2 years unless the District Court determines that release would not endanger the public health.
4. Communicable Disease rules found in 10A NCAC 41A .0205 Control Measures - Tuberculosis provide requirements for the control of tuberculosis, including American Thoracic Society references for the diagnosis and treatment of TB

Q. Incarceration Procedure

1. Isolation Orders:

- a. **"isolation"** means the authority to limit the freedom of movement **or actions** of a person with a communicable disease or communicable condition for the period of communicability to prevent the direct or indirect conveyance of the infectious agent from the person to other persons who are susceptible or who may spread the agent to others.
- b. an Isolation Order may:
 - require the person to comply with control measures, i.e., treatment orders, diagnostic tests, laboratory tests, etc., or
 - require the person to remain in their home "in isolation" until they are no longer infectious (this is also a control measure); or
 - include both of the above requirements
 - if the order includes the requirement to remain in the home until the TB nurse advises that they are not longer infectious, then the initial order is limited to 30 days. The order can be extended by the court for up to one calendar year at a time if the court determines that such extension is reasonably necessary based on a petition to the court by the health director or designee. The extension should be sought at least 3 working days before the previous order expires. (see **GS 130A-145(d)**, amended June, 2004)
- c. the Health Director issues a written Isolation Order (see **sample order at the end of this chapter**) as soon as non-compliance is exhibited. The Isolation Order must specify the following:
 - current disease status
 - required control measures and exactly how the patient is to comply with these measures
 - statutory authority for the Isolation Order and required control measures
 - statutory basis and legal steps to be taken if patient fails to comply with the Isolation Order
- d. the Health Director or designee should confer with the County Attorney, Judge, District Attorney (DA), and Public Defender regarding legal steps if the Isolation Order is violated
- e. to assure immediate sentencing, a Public Defender must be assigned to the Health Law Violator (HLV) as soon as the HLV arrest warrant is issued
- f. a HLV sent to the Department of Corrections (DOC) prior to sentencing is considered a "safe keeper" until trial and sentencing. The county will be charged a per diem fee for each day the HLV remains in safe-keeper status. Central Prison and NC Correctional Institution for Women in Raleigh are the facilities used for safe keepers if the sheriff does not believe the jail can adequately provide for the HLV.
- g. if the patient cannot be located to issue an Isolation Order, an arrest warrant should be initiated.

2. Arrest Procedure:

- a. health Director, his/her designee, and/or the County Attorney requests magistrate to swear out arrest warrant
- b. sheriff's Department arrests HLV
- c. If convicted, the HLV is sentenced "**for duration of tuberculosis disease treatment or up to two (2) years**" as determined in accordance with GS 130A-25(c).
- d. health department staff or Sheriff's Department notifies DOC of the impending arrival of the HLV by calling:
 - **DOC Transfer Coordinator at (919) 838-3739**; if no answer, press "O" and someone will answer
 - advise DOC that this is a high priority transfer, the person to be transferred is a HLV and cannot go by inmate transfer van
 - advise DOC if masks are needed when transferring HLV to prison
 - after contacting Transfer Coordinator, contact the Infection Control Coordinator for the Div. of Prisons (838-3865) and provide the same information
- e. health department should contact the Infection Control or TB nurse at the receiving facility and arrange to fax all pertinent medical information before the HLV arrives and then send copies of medical information and chest x-rays with the HLV

3. DOC Medical Management:

- a. **male** HLVs are sent to McCain Correctional Hospital. For patient information, contact Infection Control Nurse at
McCain Correctional Hospital
P.O. Box 518
McCain, N.C. 28361 - 5118
(910) 944 - 2351 (910) 944-1759 (Fax)
- b. **female** HLVs are sent to N.C. Correctional Institution for Women (NCCIW). For patient information, contact Infection Control Nurse at:
N.C. Correctional Center for Women
1034 Bragg Street
Raleigh N.C. 27610
(919) 733 - 4340 Ext. 323
- c. obtain copies of TB infection or disease treatment medical records for **released** inmates by sending a Release of Information to:

Medical Records Manager, DOP Health Services
2405 Alwin Ct, Raleigh, N.C. 27699-4268
Telephone: (919) 715-1570 or 919-715-1584
Fax: 919-715-1581

4. **DOC Health Law Violator Release from Prison Procedure (see sample letter X 2. at the end of chapter):**
 - a. The prison unit attending physician and the State TB Nurse consultant will examine the patient's record to determine that treatment has been completed prior to issuance of a release letter.
 - b. Upon determining that TB treatment has completed, the prison unit physician will send a letter (addressed to the county Health Director), to NC TB Control for the state TB Medical Director's signature. The letter will state the completion date and recommendation for release. A Community TB Referral (DC516), copies of all TB drugs received, most recent lab work, and end of treatment chest film (If applicable) will be attached to the letter to document treatment received.

5. **State Health Law Violator Release Letter Procedure**
 - a. Upon receipt of the letter and accompanying documentation from the prison unit physician, the State Health Director through NC TB Control will submit a letter concurring with the attending physician's recommendations for release.
 - b. Both letters will be sent to the county Health Director from NC TB Control.

6. **Local Health Department Health Law Violator Release from Prison Procedure**
 - a. Upon receipt of the letters and the accompanying documentation from the prison's attending physician, the county health director will review the case with the local TB clinician. The Community TB Referral (DC 516) and copies of all TB drugs received, most recent lab work, and end of treatment chest film (if applicable) will be attached to the letter documenting the completed treatment regimen.
 - b. The Health Director will prepare a similar letter addressed to the District Court judge and advise the County Attorney and DA of release request. All three (3) letters will be hand-carried to District Court to Request release of the Health Law Violator. (See sample letter X 1. at the end of this chapter.)
 - c. District Court judge will review the case and make a determination regarding an order for the Health Law Violator's release.
 - d. The court order for release is sent to the DOC Department of Combined Records:

Manager, Combined Records
2020 Yonkers Road
4226 Mail Service Center
Raleigh, NC 27699-4226
Phone: 919-716-3200 Fax 919-716-3963

R. Sample TB Treatment Agreement

TB TREATMENT AGREEMENT

Patient Name: _____ DOB _____ Date: _____

Patient Address: _____ Health Department: _____

I, _____, understand I have suspected or confirmed tuberculosis and have been prescribed by a physician to treat this disease. If my disease goes untreated, there may be serious results:

- my illness may last longer or become more severe
- I may spread TB to others
- I may develop and spread drug-resistant TB
- I can die from TB

The _____ County Health Department has the responsibility of being sure I complete treatment for my tuberculosis and do not give tuberculosis to others. To help me complete TB treatment, the health department will:

- supply all my TB medications, x-rays, and laboratory testing free of charge
- discuss with a physician any problems relating to my disease
- observe me take each dose of medicine
- see me at least monthly to evaluate for any side effects to my TB medications

To complete my treatment and protect my family, friends and co-workers I will:

- give sputum samples when asked
- keep all appointments for medical testing and x-rays
- be at the agreed-upon location to take my TB medication
- tell the health care worker whenever I plan to change my address or location

Visit Day(s): _____ Time: _____ Location: _____

If a scheduled visit falls on a holiday, the health care worker will work with me to make an adjustment in my schedule.

I have read this agreement and understand the following **(initial on line)**:

_____ Taking TB medication is very important

_____ I am responsible for the 4 tasks listed above

_____ I have been told to stop taking my medication and call my doctor and the health department if I have any side effects

_____ If I fail to complete these tasks, legal action can be taken to make sure I complete my TB treatment

_____ I have been given the North Carolina TB Control program's pamphlet, "TB and You" which lists the possible side effects of tuberculosis medicines. These possible side effects have been explained to me. I will inform the TB nurse of any problems that I may have regarding any physical complaint or possible side effects to the tuberculosis medications

Patient Signature and Date

Witness Signature and Date

S. Sample TB Treatment Agreement (Spanish)

THIS PAGE IS CURRENTLY UNDER REVISION

V. Sample Isolation Order to Limit Freedom of Movement and Access

(Health Department Letterhead)

TB ISOLATION ORDER TO LIMIT FREEDOM OF MOVEMENT AND ACCESS

I, _____, Health Director of the _____ County Health Department, pursuant to authority vested in me by N.C. General Statute 130A-145, issue this Isolation Order to _____ (patient name).

DOB: _____

You are reasonably suspected of having or confirmed to have tuberculosis disease based on diagnostic evaluation that may include history of present illness, tuberculin skin testing, radiographic findings or laboratory findings.

You have been properly informed and counseled by (name) _____, (title) _____, (agency) _____, regarding the control measures for tuberculosis disease. Failure to comply with the prescribed measures will violate N.C. General Statute 130A-144.

You are ordered to comply with the following control measures:

- You must remain in your home, and not allow access by anyone other than those who reside in the household and your health care providers, until the Health Department advises you that you are no longer infectious and are no longer restricted to the house. **(This statement can be modified if needed to address specific circumstances.)**

-
-
-
-
-

If you fail to comply with this TB Isolation Order to Limit Freedom of Movement and Access, you will be subject to prosecution for a misdemeanor offense pursuant to N.C. General Statute 130A-25 (a) and (b), punishable by up to two (2) years imprisonment, as determined in accordance with N.C. General Statute 130A-25 (c).

If you move to a new address or leave this county, you are required to notify this Health Department.

The staff of this Health Department remains available to provide assistance and counseling to you concerning your tuberculosis disease and compliance with this TB Isolation Order to Limit Freedom of Movement and Access.

Pursuant to N.C. General Statute 130A-145 (d), you may petition the superior court for review of this TB Isolation Order to Limit Freedom of Movement and Access. N.C. General Statute 130A-145 (d) states in part: "Any person substantially affected by that limitation may institute in superior court in Wake County or in the county in which the limitation is imposed an action to review that limitation. The official who exercises the quarantine or isolation authority shall give the persons known by the official to be substantially affected by the limitation reasonable notice under the circumstances of the right to institute an action to review the limitation. If a person or a person's representative requests a hearing,

W. Sample Isolation Order to Limit Freedom of Movement and Access (Spanish)
(Health Department Letterhead)

TUBERCULOSIS

Orden de Aislamiento para Limitar Libertad de Movimiento y Acceso TB Isolation to Limit Freedom of Movement and Access

Yo, _____, el director de salud del condado de _____ de acuerdo a la autoridad depositada en mí por los *Estatutos Generales de Carolina del Norte* (130A145), expido esta *Orden de Aislamiento* a _____ (patient name)

Fecha de Nacimiento: _____

Se sospecha o se ha confirmado que usted padece de tuberculosis basándonos en un diagnóstico que puede incluir su historia clínica, la prueba de tuberculina, radiografías o pruebas de laboratorio.

Usted ha sido informado y aconsejado por (name) _____
(title) _____ (agency) _____ respecto a las medidas de control que se necesitan tomar para el control de la tuberculosis. El no cumplir con las medidas de control prescritas violará las leyes de *Estatutos Generales de Carolina del Norte* (130A-144)

Se le ordena a usted el cumplir con las siguientes medidas de control:

- Usted debe permanecer en su hogar y no permitir acceso a otras personas, a excepción de aquellas que viven en su hogar y a las personas que le proporcionan los servicios de salud, hasta que el *Departamento de Salud* le informe que ya no hay peligro de infección y que no tiene que estar aislado en su casa.

(This statement can be modified if needed to address specific circumstances)

-
-
-
-

Si usted no acata esta *Orden de Aislamiento para limitar su libertad de movimiento y acceso*, usted pudiera ser acusado de un crimen menor, de acuerdo a los *Estatutos Generales de Carolina del Norte* (130A-25), y podría ser condenado a encarcelamiento hasta por dos años, tal como está determinado por los *Estatutos Generales de Carolina del Norte* (130^a-25).

Si usted se cambia de dirección o se va de este condado, se requiere que NOTIFIQUE de este cambio al Departamento de Salud.

El personal de este Departamento de Salud está disponible para ayudarle y aconsejarle en todo lo relacionado con la tuberculosis, y cómo cumplir adecuadamente con esta *Orden de Aislamiento*.

De acuerdo a los *Estatutos Generales de Carolina del Norte*, usted puede pedir a una corte superior una revisión de esta *Orden de Aislamiento para Limitar Libertad de Movimiento y Acceso*. Los *Estatutos Generales de Carolina del Norte* dicen que: "Cualquier persona que es afectada substancialmente por la limitación, puede pedir a la corte superior del condado de Wake, o en el condado donde la limitación es ordenada, que se revise la limitación impuesta. El oficial que ordenó el aislamiento o cuarentena deberá dar a las personas afectadas un aviso de cómo pueden pedir esta revisión. Si alguna persona pide una audiencia, la audiencia deberá tener lugar dentro de un periodo de 72 horas (excluyendo sábados y domingos). La persona substancialmente afectada por la

limitación, tiene derecho a ser representada por algún abogado de su elección, o si la persona es indigente, la persona pudiera ser representada por un abogado de oficio, tal como lo establece el Artículo 36 del Capítulo 7ª de los *Estatutos Generales* y las reglas adoptadas por la *Oficina de Servicios de Defensa del Indigente*”.

La validez de esta *Orden de Aislamiento para Limitar Libertad de Movimiento y Acceso*, expira en un periodo de 30 días, a menos que sea extendida o modificada por la corte, de acuerdo a los *Estatutos Generales* (130-145).

Director de Salud

Fecha

Expedido por: _____

Fecha

Recibí el original de esta orden: _____

Paciente

Fecha

X1. **Health Department:** Sample Release Letter

Dear **(District Court Judge's name)**:

Pursuant to NC GS 130A-25 (c), (Violator's name) will have completed the prescribed course of therapy for tuberculosis disease on (date). Appropriate laboratory tests confirm that she/he is no longer a danger to the public health. I have received consultation from the State Health Director, the prison unit physician and the TB Medical Consultant of the confinement facility (see attached). Therefore, I recommend that an order for his/her release be issued to be effective on (date - same date listed above).

Sincerely,

(Health Director's name), Director

(_____) County Health Department

Attachments

cc: Medical Director, Department of Corrections
McCain Correctional Hospital or North Carolina Correctional
Center for Women or Central Prison

X2. **DOC:** Sample Release Letter

Dear **(Local Health Director** of Violator's home county):

Pursuant to North Carolina General Statute 130A-25(c), (Violators name) has completed the prescribed course of therapy for tuberculosis disease on (date of last dose of medicine). Appropriate laboratory tests confirm that he/she is not longer a danger to the public health. Therefore, I recommend that you petition the District Court requesting an order for his/her release to be effective (date).

Enclosed please find a copy of his/her latest chest radiograph, laboratory reports, and medication records.

Sincerely,

Attending physician (prison)

TB Medical Director, State of NC

CC: State Health Director
Director of Health Services, DOC
Nurse Consultant, State of NC
County TB Nurse

Complete for Active Disease Only

Acid Fast Bacteriology

Date Submitted	Type of Specimen	Smear Results	Date Reported	Culture Results	Date Reported	Sensitivity	Follow-up Instruction

T. B. Medication

Preventive _____ Active Treatment _____ Reason not Started _____

Date Started	Unit	Drug	Dosage	Freq.	Route	Date Stopped	Reason Stopped

Chest X- rays

Date	Position	Results

LFT (other)

Date	Test	Normal	Abnormal	Comments

Z. First-Line TB Drugs

Drug	Doses in mg/kg (Maximum Dose) is listed in parenthesis			
	Daily		Twice weekly	
	Children	Adults	Children	Adults
INH	10 - 15 (300mg)	5 (300mg)	20 - 30 (900mg)	15 (900mg)
RIF	10 - 20 (600mg)	10 (600mg)	10 - 20 (600mg)	10 (600mg)
RBT	No data	5 (300 mg)	No data	5 (300 mg)
RPT	XXXXXXXXXX	XXXXXXXXXX	XXXXXXXXXX	10 once wkly (600 mg)
PZA	15 - 30 ¹ (2g)	15 - 30 (2g)	50 (2g)	50 (4g)
EMB	15 - 20 ² (2.5g)	15 - 20 (2.5g)	50 (2.5g)	50 (4g)

¹ The American Academy of Pediatrics 2003 Red Book gives a range of 20-40 mg/kg for PZA

² The American Academy of Pediatrics 2003 Red Book gives a range of 15-25 mg/kg for EMB

- Twice weekly regimens must be given by DOT
- INH and RIF are available as combination capsule (Rifamate) containing INH 150mg and RIF 300mg

AA. The following guidelines[†] also may be used to determine the appropriate dosing for PZA and EMB in adults:

Suggested pyrazinamide doses, using whole tablets, for adults weighing 40-90 kilograms

Weight in kg (estimated lean body wt)	40 - 55 kg	56 - 75 kg	76 - 90 kg
Daily, mg (mg/kg)	1000 (18.2 - 25)	1500 (20.0 - 26.8)	2000 ¹ (22.2 - 26.3)
Twice weekly, mg (mg/kg)	2000 (36.4 - 50.0)	3000 (40 - 53.6)	4000 ¹ (44.4 - 52.6)
Thrice weekly, mg, (mg/kg)	1500 (27.3 - 37.5)	2500 (33.3 - 44.6)	3000 ¹ (33.3 - 39.5)

¹ Maximum dose regardless of weight

Suggested ethambutol doses, using whole tablets, for adults weighing 40-90 kilograms

Weight in kg (estimated lean body wt)	40 - 55 kg	56 - 75 kg	76 - 90 kg
Daily, mg (mg/kg)	800 (14.5 - 20.0)	1200 (16.0 - 21.4)	1600 ¹ (17.8 - 21.1)
Twice weekly, mg (mg/kg)	2000 (36.4 - 50.0)	2800 (37.3 - 50.0)	4000 ¹ (44.4 - 52.6)
Thrice weekly, mg (mg/kg)	1200 (16.0 - 21.4)	2000 (26.7 - 35/7)	2400 ¹ (26.7 - 31.6)

¹ Maximum dose regardless of weight

[†] Centers for Disease Control and Prevention. Treatment of Tuberculosis. American Thoracic Society, CDC, and Infectious Diseases Society of America. MMWR 2003; 52 (No. RR-11): 5.

BB. Common Adverse Reactions to First-Line Drugs

Adverse Reactions	Signs and Symptoms	Lab Test	Usual Causes
Dermatitis	pruritus, rash, hives, fever		PZA ,RIF, INH, rarely EMB
Hepatitis	anorexia, nausea, vomiting, fatigue, dark urine, jaundice	AST, Bilirubin	INH, RIF, PZA, rarely EMB
GI upset	anorexia, nausea, vomiting, epigastric pain		PZA, RIF
Peripheral neuropathy	numbness or paresthesias of feet and hands		INH
Joint signs and symptoms	pain, swelling, tenderness, heat, redness	Uric Acid	PZA, RIF
Renal signs and symptoms	hematuria, uremia	Serum Creatinine	RIF
Hematologic manifestations	leukopenia, thrombocytopenia	CBC with platelets	RIF, INH, PZA, RBT, EMB
Uveitis	inflammation of the iris, choroid and subscleral layer of the eye		RBT
Optic neuritis	decrease in vision and/or loss, color blindness		EMB

See Chapter VI for drug interactions between TB medications and other drugs

For more information about adverse reactions and drug interactions for 1st and 2nd line tuberculosis drugs, see Centers for Disease Control and Prevention. Treatment of Tuberculosis, American Thoracic Society, CDC, and Infectious Diseases Society of America. MMWR 2003; 52 (No. RR-11). This document is available on line at http://www.cdc.gov/nchstp/tb/pubs/MMWR_TBrelated.htm; it also may be ordered from CDC on line.

CC Basic Components of TB Disease Management

- Initial diagnostic evaluation of TST, chest x-ray, bacteriology, and clinical assessment indicate active TB disease and **INH, RIF, PZA, & EMB** treatment has been initiated
- **Directly Observed Therapy is the standard of care for the treatment of disease and is required by law in North Carolina**
- MD orders must specify daily and twice weekly dosages and the duration of each drug

Weeks of Therapy	Clinical Assessment	Sputum	Chest x-ray	TST	Hepatic Function Panel >15 y/o	CBC >15 y/o	Vision while on EMB	Home Visit	TST Contacts	HIV
Baseline	x	x	x	x	x	x	x			x
1 week	x							x	x	
2 weeks		x								
4 weeks	x	x					x			
6 weeks		x								
8 weeks	x	x	x*				x		x**	
10 weeks		x								
12 weeks	x	x								
13 - 26 weeks	x document at least monthly									
26 weeks Therapy Complete	Close record		@ 2 weeks before end of therapy							

The ordered amounts of all TB medications are to be ingested in a SINGLE DOSE, according to the prescribed schedule.

Collect sputums every 2 weeks until culture negative. 85% of cases with fully susceptible Mtb should convert within 2 months of starting the INH, RIF, PZA, EMB regimen

- * Obtain a chest x-ray after 2 months of treatment for pulmonary disease if pretreatment pulmonary culture results are negative

A hepatic function panel should be obtained any time symptoms suggest hepatotoxicity. **Stop meds and notify MD** if nausea, vomiting, anorexia, rash, lethargy, fatigue, pruritus, dark urine, or jaundice occur **OR** if lab work is abnormal

- ** A second TST is indicated for TST negative **close** contacts to **infectious** TB disease

DD. International Classification System for Tuberculosis

CLASS	TYPE	DESCRIPTION
0	No TB exposure Not infected	No history of exposure Negative reaction to TST
1	TB exposure No evidence of infection	History of exposure Negative reaction to TST
2	TB infection No disease	Positive reaction to TST Negative bacteriologic studies (if done) No clinical or radiographic evidence of TB
3	Current TB disease	<u>M. tuberculosis</u> culture (if done) or Positive reaction to TST and Clinical or radiographic evidence of current disease
4	Previous TB disease	History of episode (s) of TB Or Abnormal but stable radiographic findings Positive reactions to the TST Negative bacteriologic studies (if done) And No clinical or radiographic evidence of current disease
5	TB Suspect	Diagnosis Pending

EE. Tool for Reporting Suspected or Confirmed TB Cases to TB Nurse Consultant
Within 7 Days of Notification

Date Report Faxed/Called _____ Date Suspect reported to county _____
County _____ Nurse _____
Patient's Name: _____ Gender _____ Race _____
Address: _____
DOB: _____
AFB Smear results: _____ Culture Results: _____
Specimen Source/Collection Date _____ Pulmonary _____ Extra-pulmonary _____
PPD results: _____ HIV status _____ Date tested _____
Chest x-ray results: _____

Drugs/Dosages:	Date started: _____	Weight _____
INH _____ mg	Daily _____	Bi-weekly _____
Rifampin _____ mg	Daily _____	Bi-weekly _____
PZA _____ mg	Daily _____	Bi-weekly _____
EMB _____ mg	Daily _____	Bi-weekly _____
Other _____ mg	Daily _____	Bi-weekly _____

Medical or Population Risk Factors:

Potential Drug Interactions:

Symptoms and Duration:

Contact Investigation Status (describe progress of CI, and areas of high risk, such as, children, nursing homes, schools, HIV positive contacts, etc); indicate if no contact identified

Have baseline labs been drawn? Yes _____ No _____

If HIV+: CD4 level _____ Date of most recent test _____

Additional Comments:

FF. Sample Standing Orders for Suspect/Confirmed TB Cases

Standing Order Example: Suspect or Known Tuberculosis

EXAMPLE 09/09: Intended as an example for required components only, not as best practice- all Standing Orders should reflect individual agency protocols determined by the Medical Director

Standing Order: All RNs employed or contracted by the agency that have completed orientation and have been appropriately trained in agency protocols may evaluate for signs and symptoms of tuberculosis and obtain tests.

Assessment: The patient has 2 or more of the following:

1. **Subjective Findings:**

- Night sweats
- Shortness of breath
- Chest pain
- Appetite loss
- Unexplained fatigue

2. **Objective findings:**

- Unexplained productive cough for greater than three weeks
- Hemoptysis
- Unexplained weight loss
- Unexplained fever
- Positive tuberculin skin test
- Radiologists' chest x-ray impression that indicates active tuberculosis
- Positive AFB smear

Plan of Care:

1. **Implementation:**

- Place a tuberculin skin test (TST) unless there is a documented previous positive tuberculin skin test reading
- Obtain three natural or induced sputum specimens on three consecutive days, preferably early morning specimens, and send for AFB smear, culture, and susceptibility.
- Continue to obtain sputum specimens (as described in the bullet above) every 2 weeks until there are three consecutive negative sputum cultures.
- Obtain a posterior-anterior (PA) chest x-ray on persons ≥ 5 years of age.
- Obtain both a PA and lateral view on children under the age of 5 years.
- Obtain HIV test.
- Obtain the following baseline lab test on patients ≥ 15 years old:
 - ❖ Liver function panel
 - ❖ Serum creatinine
 - ❖ CBC with differential (platelets)
- If during the treatment of tuberculosis the patient complains of signs and symptoms consistent with hepatotoxicity, such as, nausea, vomiting, loss of appetite, dark (tea or cola colored) urine, malaise, abdominal tenderness or bloating, or yellow skin or sclera, hold TB medications, and draw hepatic function panel.
- Obtain hepatic function panel monthly for the following individuals:
 - ❖ Abnormal baseline hepatic function

- ❖ Pregnant or up to 3 months postpartum
- ❖ Those with symptoms of hepatotoxicity
- ❖ Persons taking potentially hepatotoxic drugs
- ❖ Persons with chronic active hepatitis B or C
- ❖ Persons who report any alcohol intake while taking TB medications
- Obtain an end of treatment chest x-ray for patients diagnosed with pulmonary or pleural tuberculosis.

2. Nursing Action:

- Instruct the patient regarding applicable TB control measures.
- Ensure that physician reviews and signs all lab work results.

3. Criteria for Calling the Physician

- Call physician to report signs or symptoms of hepatotoxicity.
- Call physician anytime laboratory results are abnormal.
- Call physician if additional orders are needed.
- Call physician if drug resistance is reported
- Call physician if sputum cultures are still positive after 8 weeks of meds
- Call physician if clinical condition worsens

4. Follow-up:

- Follow-up with the physician for treatment orders after initial evaluation is complete.
- Evaluate the patient monthly using the Tuberculosis Flow Sheet (DHHS 2810)

Resources: NC TB Control Program Policy Manual

Legal Authority: Nurse Practice Act, G.S. 90-171.20 (7) (f) & (8) (c)

Date written: _____

Approved by: _____

Date: _____

Approved by: _____

Date: _____

Approved by: _____

Date: _____

Approved by: _____

Date: _____

Approved by: _____

Date: _____

Approved by: _____

Date: _____