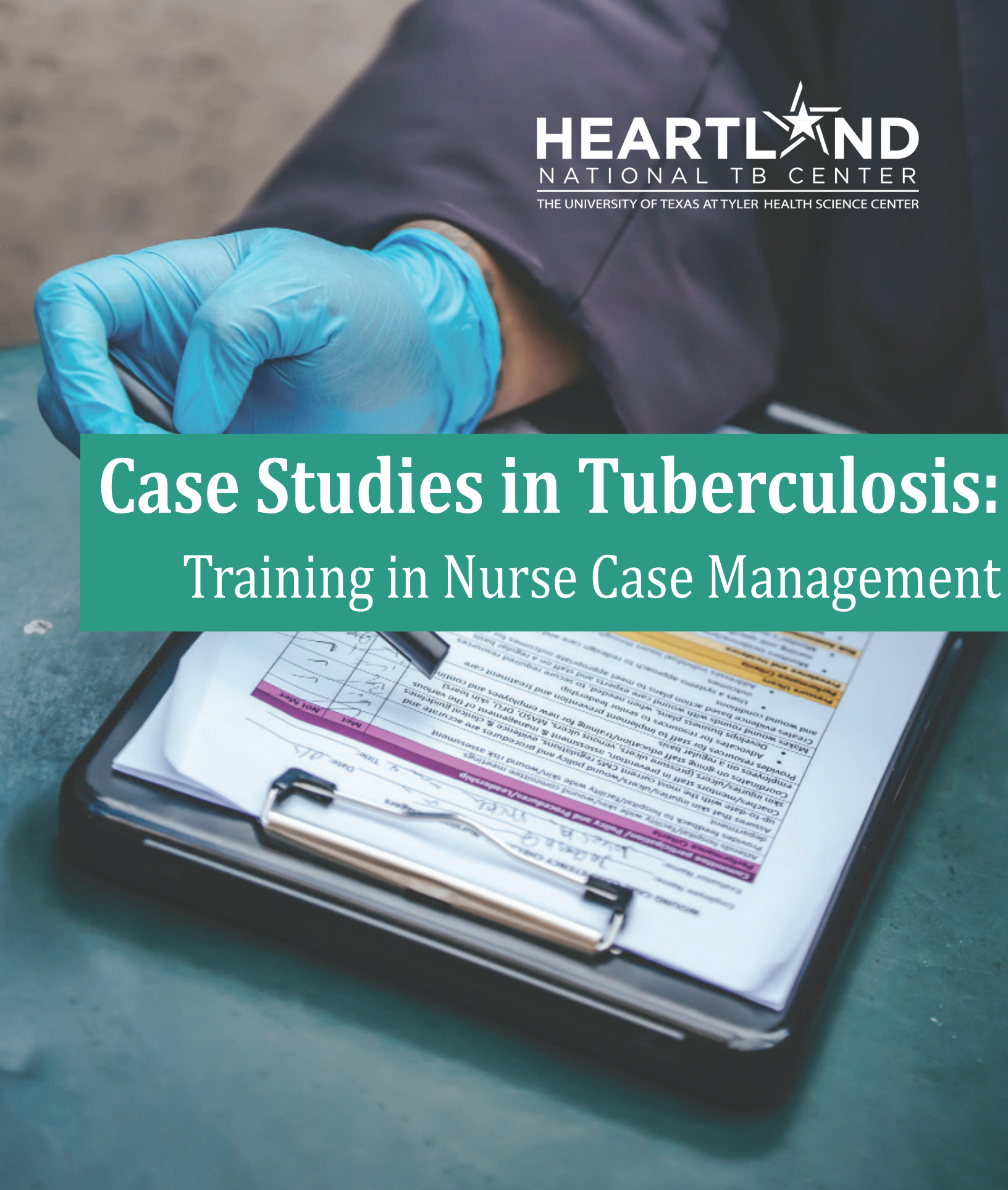

HEARTLAND
NATIONAL TB CENTER
THE UNIVERSITY OF TEXAS AT TYLER HEALTH SCIENCE CENTER

Case Studies in Tuberculosis:

Training in Nurse Case Management

EXCELLENCE | EXPERTISE | INNOVATION

Introduction

Dear Healthcare Professional,

Prior to reviewing the content of this book, it is highly recommended that you complete the Centers for Disease Control and Prevention (CDC) Self-Study Modules on Tuberculosis (TB). The modules contain basic information regarding transmission, pathogenesis, epidemiology, testing, infection control, managing adherence, patient rights, contact investigations, and outbreak detections. You can access the modules at https://www.cdc.gov/tb/education/ssmodules/default.htm.

Seldom does patient-care follow the relatively straight-forward path outlined in the CDC Self-Study Modules on TB. Due to this, the case studies in this book are designed to provide guidance and relevant reference material to gain insight into challenges faced in TB case management. Patients will often have multiple barriers to an accurate diagnosis and completion of their therapy, and thus public helath nurses must develop skills in problem-solving to successfully treat and care for a patient with TB infection or TB disease.

The studies in this new book are continue to be based on real-life experiences of TB nurses in the Heartland region and beyond. They are still designed to illustrate key concepts in TB prevention and care and can still be used to train new nurses and other healthcare providers who are inexperienced in TB nurse case management. Each of the case studies presented in this book are created to be independent of one another, and therefore, you may choose to read them sequentially or in any order you desire. This collection of nursing case studies and their accompanying tools are intended to complement a TB programs's education and training of its nursing staff. It can be incorporated into new employee introduction and training on TB nurse case management or as an individual learning tool.

It is our hope that these case studies will help the current and future generations of healthcare providers to hone their skills and enhance their knowledge within TB nurse case management for years to come. The work that healthcare professionals do on a day-to-day basis is undeniably important and affects an immeasurable number of individuals and organizations. On behalf of all those whom you will encounter in the coming years, we thank you for your time, your continued dedication to learning and self-improvement, and for allowing us to become a part of your journey.

Acknowledgments

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Table of Contents

Table of Contents

Acronyms and Abbreviations

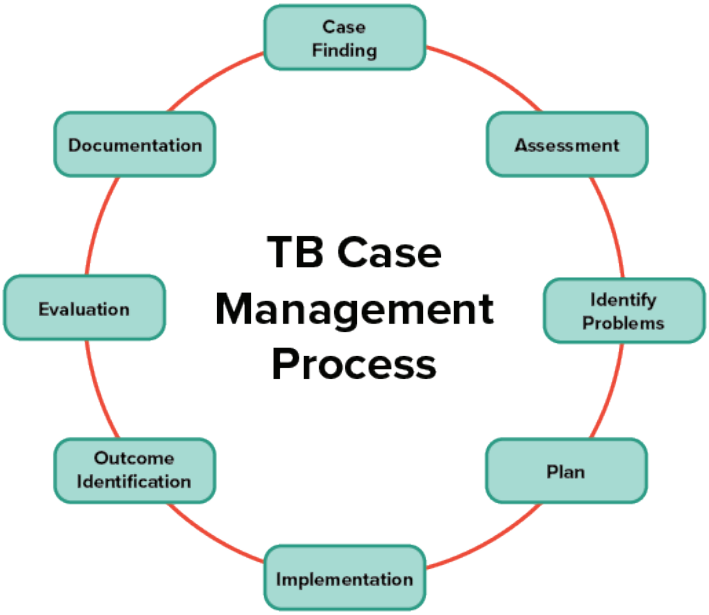
AFB	acid-fast bacilli
AII	airborne infection isolation
ALT	Alanine Aminotransferase
AST	Asparate Aminotransferase
ATS	American Thoracic Society
BCG	Bacillus Calmette–Guérin
BDQ	bedaquiline
CDC	Centers for Disease Control and Prevention
CXR	chest x-ray
DOT	directly observed therapy
DST	drug susceptibility testing
ED	emergency department
eDOT	electronic directly observed therapy
EKG	electrocardiogram
EMB	ethambutol
ER	emergency room
ESL	English as a second language
ETA	ethionamide
HCV	hepatitis C
HIV	human immunodeficiency virus
HNTC	Heartland National Tuberculosis Center
ID	infectious disease
IGRA	interferon gamma release assay
INH	isoniazid
LFTs	liver function tests
LHD	local health department
LTBI	latent TB infection
LZD	linezolid
M. tuberculosis	*Mycobacterium tuberculosis*
MDR-TB	multi-drug resistant tuberculosis
NAAT	nucleic acid amplification test
OTC	over-the-counter
PA	posteroanterior
PCP	primary care provider
PHN	public health nurse
PN	peripheral neuropathy
PZA	pyrazinamide
QFT	QuantiFERON®-TB Gold in Tube
RIF	rifampin
RIPE	tuberculosis regimen: rifampin, isoniazid, pyrazinamide, ethambutol
RPT	rifapentine
RR	rifampin-resistant
SAT	self-administered therapy
SRO	single room occupancy
TB	tuberculosis
TDM	therapeutic drug monitoring
TdP	Torsades de Pointes
TNF-α	tumor necrosis factor-alpha
T-SPOT®	T-SPOT.TB® test
TST	tuberculin skin test
VA	Veterans Affairs
vDOT	video directly observed therapy
Xpert®	Cepheid GeneXpert®

The Nursing Process

The Nursing Process is inherent to TB Nurse Case Management. TB nurses utilize this process consciously first (as a novice) then unconsciously (as a seasoned case manager) in order to deliver evidence-based practice and patient centered care.

The figure to the right serves as guide that identifies the eight steps in the TB Case Management Process and how these steps may align to the Nursing Process discussed within this book.

If at any time you need a refresher as to what components are included in each step of the Nursing Process, please use the explanations below.



Assessment

An RN uses a systematic, dynamic way to collect and analyze data about a client, the first step in delivering nursing care. Assessment includes not only physiological data, but also psychological, sociocultural, spiritual, economic, and life-style factors as well. For example, a nurse's assessment of a patient with pulmonary TB with GI upset includes not only the physical causes and manifestations, but the patient's response—an inability to get out of bed, refusal to take medications, withdrawal from family members, anger directed at health department staff or fear.

Diagnosis

The nursing diagnosis is the nurse's clinical judgment about the client's response to actual or potential health conditions or needs. The diagnosis reflects not only that the patient is experiencing GI upset, but that the symptom has caused other problems such as anxiety, poor nutrition, and conflict within the family, or has the potential to cause complications—for example, treatment failure is a potential hazard to a patient who is refusing anti-tuberculosis treatment. The diagnosis is the basis for the nurse's care plan.

Outcomes/Planning

Based on the assessment and diagnosis, the nurse sets measurable and achievable short- and long-range goals for this patient that might include moving the times the medications or meals are administer, maintaining adequate nutrition by eating smaller, more frequent meals and resolving conflict through counseling. Assessment data, diagnosis, and goals are written in the patient's care plan so that nurses (as well as other health professionals) caring for the patient have access to it.

Implementation

Nursing care is implemented according to the care plan, so continuity of care for the patient during tuberculosis therapy is assured. Care is documented in the patient's record.

Evaluation

Both the patient's status and the effectiveness of the nursing care must be continuously evaluated, and the care plan should be modified as needed. Evaluation may also involve determination of whether key guidelines were in place throughout the patient's treatment. Additionally, evaulations should consider whether patient-centered care and culturally responsive care was provided to patients at each step of the process. Since tuberculosis still carries a stigma amongst many cultures, it is imperative that nonstigmatizing language be employed within each step as well as each subsequent interaction with the patient.

Product Objectives

Overall Product Objectives

After completing this educational material, participants should be able to:

1. Describe the four elements of the nursing process.
2. Demonstrate the ability to locate and gather information through medical records review and assessment.
3. Identify potential barriers to facilitating a TB patient's plan of care to completion.
4. Prioritize problem identification and identify needed resources.
5. Deliver appropriate patient-centered interventions and evaluate outcomes.

Case Study 1
Airborne Infection Isolation (AII)

Airborne Infection Isolation (AII)

Objectives:

- List the steps in the sputum collection process.
- Identify the 5 main steps of the patient interview.
- Describe the criteria to initiate and discontinue Airborne Infection Isolation (AII) in home and hospital setting.
- Describe the criteria and correct utilization for a surgical mask and N95 respirator.

Case History:

A 47-year-old Hispanic male presents to the Emergency Department (ED) after experiencing gross hemoptysis. He has a two month history of a productive cough, night sweats and fatigue. He has lost 25 pounds in the last six weeks and currently weighs 140 pounds. He has a history of heavy alcohol use and tobacco use with a chronic smoker's cough. He is an oilfield worker and travels frequently for work. He is the sole wage earner in his household and resides with his wife and three children ages, 9, 7, and 2 years old.

The emergency room (ER) clinician orders a posteroanterior (PA) and lateral chest x-ray (CXR) and three sputa specimens to be collected for acid-fast bacilli (AFB) smear, Nucleic Acid Amplification Test (NAAT), culture, and sensitivity.

1.) The patient is taken to radiology for a CXR. Since he does not have a confirmed active tuberculosis (TB) diagnosis:

a. There is no need for him to wear a mask.
b. The patient is provided a surgical mask.
c. Since he is potentially infectious, he should wear an N-95 mask.

Upon his return from radiology, you inform the patient the ER clinician has ordered the sputum specimens to be tested for TB. The ER nurse explains to the patient that sputum is material brought up from deep in the lungs, whereas mucus from the nose or throat and saliva are not good specimens.

2.) Sputum specimens are an essential step in the medical work-up to determine if the patient has active TB, the nurse will:

a. Collect the three sputum specimens in the next hour to ensure a timely diagnosis.
b. Defer sputum collection until the morning since early AM is the best time to collect a specimen.
c. Collect one specimen immediately and ensure that two more specimens will be collected every 8 hours with one being an early morning specimen.

The ER nurse provides patient education to the patient and his wife with an infographic and written instructions on sputum collection. The patient's wife speaks only Spanish. The nurse accesses a hospital-approved website with the same information and instructions for sputum specimen collection available in different languages.

(RESOURCE: Sputum specimen collection in other languages. https://www.health.state.mn.us/diseases/tb/basics/factsheets/sputum.html#2)

3.) Match the sputum collection description to the correct method. (Please use the table "Methods of Obtaining a Sputum or Extrapulmonary Site Specimen" found below to guide your response.)

Methods of Obtaining a Sputum or Extrapulmonary Site Specimen	Method
____ Use only if there is a suspicion of TB disease and there are three negative sputum smears or induced sputum AFB results.	A. Coughing
____ Best way to obtain specimens from children who cannot produce sputum.	B. Sputum Induction
____ Use for extrapulmonary TB.	C. Bronchoscopy
____ Use for patients unable to cough up sputum to encourage deep coughing.	D. Gastric Aspiration
____ Most common method for collection of sputum.	E. Biopsy

Methods of Obtaining a Respiratory Specimen

Method	Description	Advantage	Disadvantage
Spotaneous Sputum Sample	Patient coughs up sputum into a sterile container	• Inexpensive • Easy to do	• Patient may not be able to cough up sputum without assistance or may spit up saliva instead of sputum • Health care provider must coach and supervise the patient when collecting sputum
Sputum Induction	Patient inhales a saline mist which can cause a deep cough	• Easy to do • Used to obtain sputum when coughing sputum is not productive	• Specimens may be watery and may be confused with saliva (should be labeled "induced specimen") • Requires special equipment • May cause bronchospasm
Bronchoscopy with Lavage	Bronchoscope is passed through the mouth or nose directly into the diseased portion of the lung, which is lavaged (bronchoalveolar lavage [BAL]) to obtain specimen.	• Used to obtain specimen when coughing or inducing sputum is not productive or other diagnoses are being considered • Brushings and transbronchial biopsy may also be performed	• Most expensive and invasive procedure • Requires special equipment • Must be performed by a specialist in a hospital or clinic • Requires anesthesia
Gastric Aspiration	Tube is inserted through the patient's mouth or nose and passed into the stomach to get a sample of gastric secretions that contain sputum that has been coughed into the throat and then swallowed.	Used to obtain samples in children who are not able to produce sputum when they cough	• Must be performed as soon as the patient wakes up in the morning • Patient may be required to stay in the hospital • Can cause discomfort for the patient.

Source: *CDC Core Curriculum on Tuberculosis: What the Clinician Should Know*, p. 56. https://www.cdc.gov/tb/education/corecurr/index.htm

The CXR image and report are in the patient's electronic record, and it reveals bilateral cavitary infiltrates. The public health nurse (PHN) notes the patient's sputum smear is positive; the NAAT test is pending. Cultures and drug susceptibilities are also pending. The decision is made to admit the patient to the hospital.

4.) The patient is being transferred from the ER and will be admitted to the hospital. Should he be admitted to an Airborne Infection Isolation room?

a. No, there are not any AII rooms available, so it is okay for him to go to a regular room until an AII room is available.
b. No, since we don't have a final culture indicating he has TB you don't need to isolate him until the diagnosis is confirmed.
c. Yes, he should be placed in an AII room, he has a CXR that is suggestive of active TB, clinical signs and symptoms and he is sputum smear positive.
d. It is the end of your hospital shift the incoming nurse can decide what to do.

The patient is started on the standard four drug regimen for active TB based on the *Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis*.

> Tuberculosis drugs are administered together, at one dosing to achieve maximal peak serum concentrations, to facilitate DOT and decrease the risk of acquired drug resistance. (2016 ATS/CDC/IDSA *Guidelines for Treatment of Drug-Susceptible TB,* p. 22)

The hospital infection prevention nurse notifies the state health department per state statute, typically within 24 hours, of a patient with active TB disease. The plan is to discharge the patient in the next 72 hours. The PHN plans a hospital visit to interview the patient and coordinate discharge. As part of the pre-interview activities, the PHN reviews the patients' medical record, establishes a preliminary infectious period, develops an interview plan, and arranges to interview the patient at the hospital.

When the PHN arrives at the patient's room, she introduces herself as the TB nurse case manager from the local health department and shows the patient her picture ID. The PHN explains to the patient the plan to discharge him home within a couple of days, and she is there to help coordinate and ensure he has a safe discharge. She provides written and verbal information about active TB including the medications used to treat TB, home isolation, and the need for a contact investigation. She allows adequate time for the patient and his wife to ask questions and addresses any concerns. She leaves her health department business card with contact information.

The patient is discharged home the next day. Since he is still infectious, his three children are staying with the maternal grandmother in another residence. He was instructed to not travel outside the home until released from home isolation by the health department. Sputa were obtained by the local health department during his first week home of which two of the three results are still sputum smear positive (1+, 2+, smear negative). However, his cough has improved, has gained 5 pounds, and has increased energy.

At week 3, the patient has three consecutive sputum smear negative specimens and is considered non-infectious. In order to be considered non-infectious, the patient must meet all of the following criteria: have three consecutive negative AFB sputum smears collected in 8- to 24-hour intervals (at least one being an early morning specimen); their symptoms have improved clinically (for example, they are coughing less, and they no longer have a fever); and they are adherent with an adequate treatment regimen for two weeks or longer.

He is released from home airborne infection isolation and returns to work. He works long hours in the oil field and is not available for directly observed treatment (DOT) during normal public health clinic hours. In consideration of the patient-centered care model approach, the case manager explores options for administering TB medications for this patient.

5.) What are options for medication administration to explore with the patient?

a. Electronic DOT
b. Self-administered therapy is acceptable since he is non-infectious
c. Insist that he must come to the HD daily for DOT
d. Arrange for a mutually agreeable time and location where you can meet the patient daily for DOT.
e. A or D

> Electronic DOT is an alternate form of directly administered treatment and should not be seen as an award for patient adherence.

QUESTIONS AND ANSWERS

1.) The patient is taken to radiology for a CXR. Since he does not have a confirmed active TB diagnosis:

a. There is no need for him to wear a mask.

b. The patient is provided a surgical mask.

c. Since he is potentially infectious, he should wear an N-95 mask.

Rationale: Since the patient is sputum smear positive and has a clinical history suggestive of TB, he is considered potentially infectious. To prevent droplet nuclei from being expelled into the air, patients with infectious TB should wear a surgical mask. An N-95 mask (personal respirator) is utilized by health care workers or other persons in contact with a potentially infectious patient to prevent inhalation of droplet nuclei.

Source: *CDC TB 101 for Health Care Workers, "*Lesson 2: TB Transmission and the Development of TB Disease*."* https://www.cdc.gov/tb/webcourses/tb101/page1796.html#:~:text=CDC%20%2D%20TB%20101%20%2D%20Infection%20Control%20%2D%20Web%20Courses%20%2D%20TB&text=Personal%20respirators%20should%20be%20worn,being%20expelled%20into%20the%20air

2.) Sputum specimens are an essential step in the medical work-up to determine if the patient has active TB, the nurse will:

a. Collect the three sputum specimens in the next hour to ensure a timely diagnosis.

b. Defer sputum collection until the morning since early AM is the best time to collect a specimen.

c. Collect one specimen immediately and ensure that two more specimens will be collected every 8 hours with one being an early morning specimen.

Rationale: Performing three AFB smears confirms pulmonary TB with a sensitivity of approximately 70%. The reason for performing three AFB smears is that each specimen increases sensitivity. The sensitivity of a first morning specimen is 12% greater than a single spot specimen. During specimen collection, the PHN should wear a properly fit tested N-95 respirator and confirm there is negative airflow in the patient's Airborne Infection Isolation (AII) room.

Source: ATS/IDSA/CDC. (2016). *Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children*, p. 16. https://www.cdc.gov/tb/publications/guidelines/pdf/cid_ciw694_full.pdf

CDC Core Curriculum on Tuberculosis: What the Clinician Should Know, p. 143. https://www.cdc.gov/tb/education/corecurr/index.htm

3.) Match the sputum collection description to the correct method. (Please use the table "Methods of Obtaining a Sputum or Extrapulmonary Site Specimen" found below to guide your response.)

Methods of Obtaining a Sputum or Extrapulmonary Site Specimen	Method
C Use only if there is a suspicion of TB disease and there are three negative sputum smears or induced sputum AFB results.	A. Coughing
D Best way to obtain specimens from children who cannot produce sputum.	B. Sputum Induction
E Use for extrapulmonary TB.	C. Bronchoscopy
B Use for patients unable to cough up sputum to encourage deep coughing.	D. Gastric Aspiration
A Most common method for collection of sputum.	E. Biopsy

Rationale: All persons suspected of having TB disease at any site should have sputum specimens collected for an AFB smear and culture, even persons without respiratory symptoms. There are four methods for obtaining a sputum specimen. Review the following table on methods for sputum collection. Sputum collection in home and/or hospital facility. Ideally, all three sputum collections should be observed. However, at a minimum, at least the first specimen should be observed.

Source: *CDC Core Curriculum on Tuberculosis: What the Clinician Should Know,* p. 56. https://www.cdc.gov/tb/education/corecurr/index.htm

4.) The patient is being transferred from the ER and will be admitted to the hospital. Should he be admitted to an Airborne Infection Isolation room?

a. No, there are not any AII rooms available, so it is okay for him to go to a regular room until an AII room is available.

b. No, since we don't have a final culture indicating he has TB you don't need to isolate him until the diagnosis is confirmed.

c. Yes, he should be placed in an AII room, he has a CXR that is suggestive of active TB, clinical signs and symptoms and he is sputum smear positive.

d. It is the end of your hospital shift the incoming nurse can decide what to do.

Rationale: A patient that is sputum smear positive with clinical symptoms of TB is considered infectious and should be placed in an AII room.

Source: Centers for Disease Control and Prevention. *Guidelines for Preventing the Transmission of* Mycobacterium tuberculosis *in Health-Care Settings*. MMWR: December 30, 2005; Volume 54 (RR17). https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5417a1.htm?s_cid=rr5417a1_e p.20

5.) What are options for medication administration to explore with the patient?

a. Electronic DOT
b. Self-administered therapy is acceptable since he is non-infectious
c. Insist that he must come to the HD daily for DOT
d. Arrange for a mutually agreeable time and location where you can meet the patient daily for DOT.
e. A or D

Rationale: The patient-centered care model and case management respect the individual's right to participate actively as an informed partner in decisions and activities related to TB diagnosis and treatment.

Source: ATS/CDC/IDSA. (2016). *Guidelines for Treatment of Drug-Susceptible TB*, p. 15. https://www.cdc.gov/tb/publications/guidelines/pdf/Clin-Infect-Dis.-2016-Nahid-cid_ciw376.pdf

Airborne Infection Isolation (AII)

Notes:

Case Study 2
Contact Investigation

Contact Investigation

Objectives:

- Describe the contact investigation process.
- Calculate the infectious period for a person with TB.
- Explain how to prioritize TB contacts.

Case History:

A 22-year-old woman presents to the emergency department (ED) on May 4th with fever, cough, and hemoptysis. She was born in China, has been in the United States for five years, and is currently a student at a local college. She reports an 11-pound weight loss and a productive cough for the last three months. She visited an urgent care facility on March 7th, was diagnosed with pneumonia, and prescribed levofloxacin. Based on her chest X-ray (CXR), signs and symptoms, and tuberculosis (TB) endemic country of origin, the ED clinician suspects pulmonary TB. She is admitted to the hospital and placed in an airborne infection isolation (AII) room.

The hospital infection control practitioner notified the local public health nurse (PHN) of the patient's suspected TB diagnosis. The PHN follows the ten steps of conducting a contact investigation (found on page 21), uses a TB Contact Investigation Checklist (found on page 22), and arranges a visit to the hospital to meet the patient in order to conduct the initial contact investigation interview and discuss the patient's treatment.

1.) Which of the following pre-interview activities should the PHN complete? (Circle all that apply.)

a. Review the patient medical record
b. Develop a plan for directly observed therapy (DOT) on the patient's release from the hospital
c. Estimate the degree of infectiousness

The PHN continues the pre-interview activities by calculating the preliminary infectious period. Medical records reveal that her CXR at the ED showed multiple cavities in the right upper lobe. The nucleic acid amplification test (NAAT) performed at the hospital is positive for *Mycobacterium tuberculosis* (*M. tuberculosis*), and the sputum smear result is 3+.

> **Infectious Period**
> the time during which a TB case is potentially capable of trasmitting *M. tuberculosis*

2.) Using the table provided, what is the preliminary infectious period for this patient?

a. February 4th - May 4th
b. March 7th - May 31st
c. November 4th - May 4th
d. January 1st - March 7th

Recommendations for Estimating the Start of the Infectious Period

Characteristic of Case			Recommended Minimum Beginning of the Infectious Period
Respiratory TB Symptoms	Sputum Smear Positive	Pulmonary Cavity on Chest X-ray	
Yes	No	No	3 months before symptom onset or first finding consistent with TB disease, whichever is longer
Yes	Yes	Yes	3 months before symptom onset or first finding consistent with TB disease, whichever is longer
No	No	No	1 month (4 weeks) before date of suspected diagnosis
No	Yes	Yes	3 months before finding consistent with TB disease

Source: *CDC Self-Study Module on Tuberculosis*, Module 8: Contact Investigations for Tuberculosis, p. 26

Contact Investigation

The PHN went to the hospital for an initial TB interview with the patient for information and education exchange. Although the medical record indicates that the patient had a productive cough for three months, when asked more about her symptom onset, she verbalized that she first noticed coughing and feeling very tired around December 31st and remembers not feeling well enough to go out for New Year's Eve with her friends. With this updated information, the PHN revises the preliminary infectious period, which was based on the initial report of symptom onset three months before her hospital admission. The refined infectious period is now October 1st - May 4th.

The PHN continues with the contact identification stage of the TB interview, collecting information regarding home, work, college, and social settings. The patient reports she lives with a friend in an apartment close to campus, is in her last year of college, and is taking two online classes and an independent study. This semester she babysits 4-year-old twins for one of her professors two afternoons a week from 3 pm to 6 pm and visits an elderly friend about once a month for dinner while mentioning that the woman is frail and on dialysis. She also mentions she has part time job as a lifeguard at an outdoor pool once a week.

The PHN provides TB patient education, and she answers the patient's questions and concerns while ensuring that all information shared will remain private and confidential, unless mitigating circumstances arise during which her information will remain legally protected. The PHN concludes the interview and schedules the next visit before reiterating the next steps she will be taking.

3.) Which of the following following next steps should the PHN take?

Action	YES or NO
Prioritize contacts for assessment	
Coordinate a medical evaluation (with chest X ray) of the 4-year-old twins	
Go to the college and post signs indicating there was a recent TB exposure and ask people to come to the health department for testing	
Reach out to the roommate to tell her she may have been exposed to TB and ask her to come to the health department for assessment	
Plan for a re-interview with the patient and a home visit	
Plan to assess some of the patient's close contacts	

The PHN does a site visit at the college and confirms the patient's schedule. The dean shares that as part of the patient's independent study, she also meets twice a month with her advisor, who has been out sick with bronchitis for the last 2 weeks. At the pool, the PHN finds that when the patient works, she sits on a lifeguard stand by herself. The other lifeguard on duty at the same time is on a different stand at the other end of the pool and weekly staff meetings are conducted outside.

"The PHN should prioritize contacts for testing and evaluation based on:
- Likelihood of transmission including the patient's degree of infectiousness and frequency, duration, and environment of potential exposure (e.g., room size, air circulation, and proximity to the person with infectious TB)
- The contact's risk for development of TB disease (e.g., age or medical conditions that suppress the immune system, such as HIV infection); priority should be given to identifying and evaluating children younger than 5 years of age"

4.) Based on the information you have collected, classify the following people in terms of their priority for testing and evaluation:

Persons	Priority (HIGH, MEDIUM, LOW, or NOT CONTACTS)
a. The children she babysits	
b. The other lifeguards	
c. Her advisor	
d. The elderly friend	
e. All the students in college	
f. Students that shared classes with the patient last year	
g. Her roommate	

The 4-year-old twins were promptly evaluated by a pediatrician. Their initial interferon gamma release assay (IGRA) results were negative. They had no signs or symptoms of active TB, and their chest x-rays were normal. They were placed on window prophylaxis until their second IGRA test eight weeks after their last known exposure. The second IGRA results for both children were also negative. The clinician determined they were not infected with TB, and window prophylaxis was discontinued.

The roommate had documentation of a previous positive TB test result but had not been treated for latent tuberculosis infection (LTBI). She was evaluated at the health department; TB disease was excluded. She agreed to start LTBI treatment and successfully completed LTBI treatment. The elderly friend had a negative TB test.

All of them received an initial test and a repeat test 8 to 10 weeks after their last exposure.

The patient's college advisor was evaluated promptly since he was on a tumor necrosis factor-alpha (TNF-α) inhibitor and at increased risk for progression to TB disease. He was diagnosed with pulmonary TB, and a second contact investigation was initiated.

Based on the results of testing of high-priority contacts, the contact investigation was not expanded to include a wider group of contacts, such as the other lifeguards at the pool or classmates from the previous semester.

> Using a patient-centered approach to address patient concerns, providing education, answering questions, and emphasizing that TB can be cured will help to alleviate concerns and start to build the trust and rapport that is needed during TB nurse case management and contact investigation. Additionally, be sure to consider the patient's history, culture, and health beliefs as these factors may impact their approach to treatment.

The Ten Steps of a Contact Investigation

1. Review the existing information
2. Determine an initial estimate for the infectious period and estimate the degree of infectiousness
3. Interview the case
4. Review information and develop a plan for the investigation
5. Refine the infectious period and degree of infectiousness
6. Prioritze contacts
7. Conduct field visits
8. Conduct contact assessments
9. Determine whether to expand or conclude an investigation
10. Evaluate the contact investigation activities

Contact Investigation

Pre-Interview Activities

- Review medical record
- Establish preliminary infectious period
- Develop an interview plan
- Arrange interview time and place

A. Introduction

- Introduce self
- Provide identification
- Explain role in TB control
- Build trust and rapport
- Explain the purpose of the interview
- Ensure confidentiality

B. Information and Education Exchange

1. Observe case's physical and mental state, body language, and communication skills
2. Collect and confirm the following information:

___ Name	___ Next of kin	___ Medical provider for TB
___ Alias(es)/nicknames	___ Other locating information	___ Transportation availability
___ Date of birth	___ Physical description	___ Other medical conditions
___ Address	___ Known exposure to TB	___ Outpatient DOT plan
___ Telephone number	___ Recent hospitalization(s) for TB	___ Barriers to adherence

3. Assess disease comprehension/provide TB education
4. Obtain and confirm TB symptom history
5. Discuss the cases's current diagnosis
6. Discuss disease intervention behaviors, infection control, and medical appointments
7. Refine infectious period and review with the case

C. Contact Identification

- Focus on infectious period
- Explain priority and non-priority contacts
- Stress importance of identification of all contacts
- Collect information on case's contacts in the household, workplace, school, congregate settings, and social/recreational environments during the infectious period
- Information about contacts should include:

___ Name	___ Address	___ Physical description
___ Alias(es)/nicknames	___ Telephone number	___ Hours of exposure per week
___ Age, race, sex	___ Other locating information	___ Dates of first and last exposures

D. Conclusion of the Interview

- Request, then answer the case's questions
- Review and reinforce the adherence plan
- Restate next appointment (if known)
- Arrange reinterview and home visit (if not already completed)
- Leave your name and telephone number
- Thank the case and close the interview

QUESTIONS AND ANSWERS

1.) Which of the following pre-interview activities should the PHN complete? (Circle all that apply.)

a. Review the patient medical record

b. Develop a plan for directly observed therapy (DOT) on the patient's release from the hospital

c. Estimate the degree of infectiousness

Rationale: Gather information by reviewing the patient medical record, collecting information that includes onset of TB signs and symptoms including details on diagnosis, CXR report, NAAT results, AFB smear results, and demographic and social information.

Source: *CDC Self-Study Module on Tuberculosis*, "Module 8: Contact Investigations for Tuberculosis," p. 26

2.) Using the table provided, what is the preliminary infectious period for this patient?

a. February 4th - May 4th

b. March 7th - May 31st

c. November 4th - May 4th

d. January 1st - March 7th

Recommendations for Estimating the Start of the Infectious Period

Characteristic of Case			Recommended Minimum Beginning of the Infectious Period
Respiratory TB Symptoms	Sputum Smear Positive	Pulmonary Cavity on Chest X-ray	
Yes	No	No	3 months before symptom onset or first finding consistent with TB disease, whichever is longer
Yes	Yes	Yes	3 months before symptom onset or first finding consistent with TB disease, whichever is longer
No	No	No	1 month (4 weeks) before date of suspected diagnosis
No	Yes	Yes	3 months before finding consistent with TB disease

Rationale: The infectious period can be estimated as beginning 3 months prior to symptom onset or first finding consistent with TB, whichever is longer. The patient reported her symptoms started 3 months before her hospital admission on May 4th, the PHN would go back 3 months before February 4th. Thus, the preliminary infectious period begins on November 4th. Since she was placed in an isolation room on her hospital admission, the infectious period ends on May 4th.

Source: *CDC Self-Study Module on Tuberculosis*, "Module 8: Contact Investigations for Tuberculosis," p. 20-22

3.) Which of the following following next steps should the PHN take?

Action	YES or NO
Prioritize contacts for assessment	YES
Coordinate a medical evaluation (with chest X ray) of the 4-year-old twins	YES
Go to the college and post signs indicating there was a recent TB exposure and ask people to come to the health department for testing	NO
Reach out to the roommate to tell her she may have been exposed to TB and ask her to come to the health department for assessment	YES
Plan for a re-interview with the patient and a home visit	YES
Plan to assess some of the patient's close contacts	YES

Rationale: After reviewing information from the interview, an investigation plan should be developed. This will include prioritizing contacts, conducting field visits, and completing contact assessments. Since children younger than 5 can develop severe forms of TB (such as TB meningitis) very quickly, it is essential that they be fully evaluated by a pediatrician as soon as possible. Nurse case managers should also provide education regarding the signs and symptoms of TB, the importance of determining window prophylaxis, and repeat testing. Conducting a re-interview in the patient's home allows for additional discussion with the patient to identify any contacts they may have missed originally, as well as allowing the PHN to observe the home setting for any other potential contacts.

Source: *CDC Self-Study Module on Tuberculosis*, "Module 8: Contact Investigations for Tuberculosis," p. 20

4.) Based on the information you have collected, classify the following people in terms of their priority for testing and evaluation:

Persons	Priority (HIGH, MEDIUM, LOW, or NOT CONTACTS)
a. The children she babysits	HIGH
b. The other lifeguards	LOW
c. Her advisor	HIGH
d. The elderly friend	HIGH
e. All the students in college	NOT CONTACTS
f. Students that shared classes with the patient last year	LOW
g. Her roommate	HIGH

Rationale: Children and others with certain medical conditions are high-risk for progression to TB disease are considered a high priority. The elderly friend might not normally be given priority since she spends limited time with the patient; however, since she is on dialysis, she would also be a high priority. The patient's advisor might not normally be considered a priority, but since he has been out with bronchitis, it is determined that he is a high priority because he has some symptoms that could be consistent with TB. Household contacts, such as the patient's roommate, are also considered a high priority.

Contact Investigation

Since the other lifeguards did not spend much time with the patient and all time was spent outside, they are considered low-risk and are not a priority. The group of all students in the college would NOT be considered contacts. The patient is only taking online classes this semester; however, since her infectious period started in October of last year, it is possible that some of the students she was in class with last year might be considered a priority. Therefore, while this group isn't necessarily a high priority at this point in time, they might be prioritized later after all of the current high priority contacts have been evaulated and test results show transmission has occurred.

Source: *CDC Self-Study Modules on Tuberculosis, "*Module 8: Contact Investigations for Tuberculosis," p. 48-49

Centers for Disease Control and Prevention. *Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis; Recommendations from the National Tuberculosis Controllers Association and CDC*. MMWR: December 16, 2005; Volume 54 (RR15). https://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf

Notes:

Contact Investigation

Notes:

Case Study 3

TB Infection Adverse Drug Reaction

TB Infection Adverse Drug Reaction

Objectives:

- List persons at high risk for exposure to TB and progression to active tuberculosis (TB) disease.
- Describe the preferred and alternative regimens for treating latent TB infection (LTBI).
- List potential adverse reactions to medications utlized for LTBI.
- List laboratory tests and results utlized for monitoring persons on treatment for LTBI.
- Describe how to calculate proportion of LTBI doses when switching regimens.

Case History:

A 32-year-old female with a past medical history of psoriatic arthritis consulted with her primary care physician (PCP) about using tumor necrosis factor-alpha (TNF-α) blockers. She recently noticed an advertisement on TV about biologic medications that may help with her joint pain and dry, scaly skin caused by her psoriatic arthritis. The American College of Rheumatology states that TNF is a protein in your body that causes inflammation, and TNF inhibitors are drugs that help to stop the inflammation. TB testing should be done before starting this type of medication. The PCP agreed that TNF-α blockers may help her psoriatic arthritis and made a referral for her to go the local health department (LHD) for TB testing. The Public Health Nurse (PHN) at the LHD completes a TB assessment prior to TB testing and identifies that the patient is U.S. born and is a stay-at-home mother of two children with no known risk factors for TB exposure.

The PHN is aware that certain populations are at higher risk for exposure to TB and should be tested.

1.) Using the table below, check "YES" or "NO" if TB testing should be done for this following populations.

Persons with the following risk factors should be tested for TB?	YES	NO
Birth or residence in a country with a high or medium incidence rate of TB, regardless of year of arrival		
All Health Care personnel in a hospital or clinic setting annually		
Close Contact of someone with infectious TB disease		
Immunosuppression, current or planned		
Certain medical conditions or social circumstances that meet state or local criteria		

An interferon gamma release assay (IGRA) is drawn, and the T-SPOT.TB® (T-SPOT®) test is positive. Per the health department's standing orders from the TB medical director, patients with positive IGRAs are referred for a chest X-Ray (CXR). The PHN reviews the TB symptom checklist for active TB with the patient. Signs and symptoms of active TB include prolonged cough, hem-optysis, fever or chills, night sweats, unintended weight loss, fatigue and chest pain. The patient denies all symptoms and states she doesn't know where she could have been exposed to TB.

Her CXR is normal. The PHN completes baseline laboratory tests, AST, ALT, CBC and opt-out HIV testing per the health department's standing orders from the TB medical director for persons starting treatment for LTBI. At the completion of the pre-treatment clinical evaluation, active TB disease is excluded, and LTBI is diagnosed by the clinician.

> Some Health departments utilize standing orders written by a medical doctor, for nurses to implement in designated situations. Check with your HD to determine what is the policy and protocol for your institution.

The patient is eager to start treatment for LTBI so that she can start a TNF-α blocker and get some pain relief. Her joints have become increasingly swollen and painful, and she has difficulty caring for her two young children. The PCP indicated that she could start the TNF-α blocker after one month of LTBI treatment.

Regimens are ranked in the 2020 *Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC* based on tolerability and effectiveness from randomized controlled trials. The regimens are ranked as preferred or alternative.

- **Preferred regimens:** excellent tolerability and efficacy, shorter treatment duration, and higher completion rates
- **Alternative regimens:** excellent efficacy but longer treatment duration, and lower completion rates

2.) Please indicate if the treatment regimen is preferred or alternative according to the 2020 *Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC*.

Regimen	Priority Rank PREFERRED or ALTERNATIVE?
3HP: 3 months of isoniazid (INH) and rifapentine (RPT) once weekly	
4R: 4 months of rifampin (RIF) daily	
3HR: 3 months of INH and RIF daily	
6H: 6 months of INH daily	
9H: 9 months of INH daily	

The clinician orders 3HP: 3 months of INH and RPT once weekly.

3.) Which of the following are precautions patients should be informed of while taking treatment for LTBI?

a. Patients on hormonal contraceptives should be encouraged to continue hormonal contraception, in addition a barrier method should be used.
b. Due to risk of hepatotoxicity patients should limit usage of acetaminophen, alcohol and other potentially liver toxic substances.
c. Orange/red discoloration of body fluids may occur.
d. If the patient experiences any side effects, the medication should be promptly discontinued, and the health care practitioner notified.
e. All of the above.

TB Infection Adverse Drug Reaction

The PHN arranges for the patient to come to the health department once a week for directly observed treatment (DOT). The patient assures the PHN that she will take her TB medications because she really wants to start treatment for her psoriatic arthritis.

4.) The TB nurse case manager explains that DOT...

a. is the standard of care for intermittent TB infection regimens.
b. allows opportunity for the nurse to assess for side effects related to the medications.
c. is more effective than self-administered treatment (SAT).
d. A and B

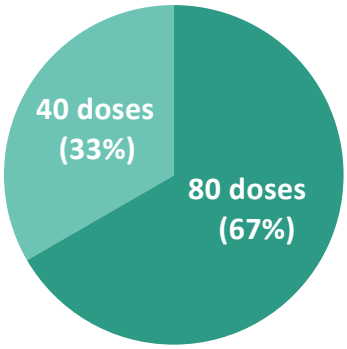
When the patient comes to the LHD for 3HP dose #5, the PHN notices that the patient's eyes are jaundiced, and she seems to be quite tired. When queried about how she is feeling the patient denies any side effects. The PHN holds the 3HP dose and contacts the clinician, and a CBC and CMP are drawn. Later that afternoon the lab tests are returned. Her AST is 350 U/L and ALT is 400 U/L. Upon further conversations with the patient, the PHN discovers that she had been taking high doses of acetaminophen due to her increased joint pain.

The 3HP treatment regimen was held until the patient's LFTS returned to normal. The clinician decided to discontinue 3HP and start the patient on RIF only. The clinician determined that the INH coupled with high doses of acetaminophen caused the liver toxicity.

To minimize the overall duration of treatment, some experts when switching from one regimen to another calculate the number of doses needed to complete treatment with a different regimen. To determine the number of doses needed with the second regimen the following should be done:

1. Count the doses taken during the first regimen.
2. Calculate the proportion of the first regimen that was completed.
3. Subtract the proportion of the regimen completed from 100%.
4. Multiply the percentage of the first regimen that was not completed by the number of doses for the full second regimen. The result will be the number of doses needed to complete treatment in the second regimen.

The patient completed 4 out of 12 weeks of **3HP** (i.e. 33% of total doses).



100% of total needed doses - 33% of already completed doses = 67% to be completed.

4R is a four-month of daily RIF regimen of 120 doses.

120 doses x 67% = 80 doses of 4R to be completed, which equates to approximately 2 ½ months of daily RIF to complete for a full LTBI treatment regimen.

TB Infection Adverse Drug Reaction

In this case study, the patient wanted to complete her treatment for LTBI so strongly that she may have underplayed the severity of her liver toxicity symptoms. The LHD was able to provide video DOT (vDOT) with the regimen change to rifampin daily, this ensured monitoring for liver toxicity and adherence to the treatment regimen.

> When addressing patient adherence, the focus is on the potential for non-adherence to the treatment regimen. It is important to be aware of and explore the patient's motivation for treatment.

QUESTIONS AND ANSWERS

1.) Using the table below, check "YES" or "NO" if TB testing should be done for this following populations.

Persons with the following risk factors should be tested for TB?	YES	NO
Birth or residence in a country with a high or medium incidence rate of TB, regardless of year of arrival	X	
All Health Care personnel in a hospital or clinic setting annually		X
Close Contact of someone with infectious TB disease	X	
Immunosuppression, current or planned	X	
Certain medical conditions or social circumstances that meet state or local criteria	X	

Rationale: Populations recommended to receive TB testing are those persons from countries with high or medium incidence rate due to the increased risk of exposure and infection with TB disease in their country of birth/residence.

The American College of Occupational and Environment Medicine (ACOEM) and National TB Controller's Association (NTCA) endorse the discontinuation of routine annual TB testing in healthcare personnel (HCP) and the increased emphasis on the role of occupational health in encouraging treatment of persons with LTBI to prevent progression to active disease (reactivation) and to positively impact the public's health.

Persons immunosuppressed or going on immunosuppression therapy have a greater risk of progression to active TB if they are infected with TB. Therefore, TB testing is recommended to determine their status and provide treatment for TB infection.

Source: National TB Controller's Association. (2021). *Testing and Treatment of Latent Tuberculosis Infection in the United States: Clinical Recommendations*. p. 17. https://www.tbcontrollers.org/resources/tb-infection/clinical-recommendations/

Centers for Disease Control and Prevention. *Tuberculosis Screening, Testing, and Treatment of U.S. Health Care Personnel: Recommendations from the National Tuberculosis Controllers Association and CDC*. MMWR: May 17, 2019; Volume 68 (19). https://www.cdc.gov/mmwr/volumes/68/wr/mm6819a3.htm

American College of Occupational and Environment Medicine. *Tuberculosis Screening, Testing, and Treatment of US Health Care Personnel: ACOEM and NTCA Joint Task Force on Implementation of the 2019 MMWR Recommendations*. JOEM: July, 2020; Volume 62 (7). https://acoem.org/acoem/media/PDF-Library/Publications/Tuberculosis_Screening,_Testing,_and_Treatment.pdf

2.) Please indicate if the treatment regimen is preferred or alternative according to the 2020 *Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC*.

Regimen	Priority Rank PREFERRED or ALTERNATIVE?
3HP: 3 months of isoniazid (INH) and rifapentine (RPT) once weekly	**PREFERRED**
4R: 4 months of rifampin (RIF) daily	**PREFERRED**
3HR: 3 months of INH and RIF daily	**PREFERRED**
6H: 6 months of INH daily	**ALTERNATIVE**
9H: 9 months of INH daily	**ALTERNATIVE**

Source: Centers for Disease Control and Prevention. *Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC*. MMWR: February 14, 2020; Volume 69 (1). https://www.cdc.gov/mmwr/volumes/69/rr/rr6901a1.htm

3.) Which of the following are precautions patients should be informed of while taking treatment for LTBI?

a. Patients on hormonal contraceptives should be encouraged to continue hormonal contraception, in addition a barrier method should be used.
b. Due to risk of hepatotoxicity patients should limit usage of acetaminophen, alcohol and other potentially liver toxic substances.
c. Orange/red discoloration of body fluids may occur.
d. If the patient experiences any side effects, the medication should be promptly discontinued, and the health care practitioner notified.
e. All of the above

Source: National TB Controller's Association. (2021). *Testing and Treatment of Latent Tuberculosis Infection in the United States: Clinical Recommendations*. p. 100-111. https://www.tbcontrollers.org/resources/tb-infection/clinical-recommendations/

4.) The TB nurse case manager explains that DOT...

a. is the standard of care for intermittent TB infection regimens.
b. allows opportunity for the nurse to assess for side effects related to the medications.
c. is more effective than self-administered treatment (SAT).
d. A & B

Rationale: Nurse case management, the use of incentives and enablers, and treatment administration by DOT have proven to be an effective triad to provide patient-centered care for safe and documented completion of LTBI treatment. Nurse-guided treatment management has been a model successfully used in public health to promote safety during treatment and increase treatment completion rates for persons with LTBI. Health care providers treating patients with LTBI are encouraged to use existing nurse case management services in their community to which their patients may have access or to create new nurse case management programs in their own facilities.

TB Infection Adverse Drug Reaction

Notes:

TB Infection Adverse Drug Reaction

Notes:

Case Study 4

TB Treatment in a Patient at Risk for Hepatotoxicity

TB Treatment in a Patient at Risk of Hepatotoxicity

Objectives:

- List the factors that increase a patient's risk of hepatoxicity while on tuberculosis (TB) treatment.
- Describe the monitoring process for patients who have an increased risk of hepatotoxicity.
- Identify the signs and symptoms of hepatotoxicity.
- Discuss managing TB treatment in patients who experience hepatotoxic effects while on TB treatment.

Case History:

The patient is a 65-year-old male Air Force veteran with a right-sided below the knee amputation and a history of untreated hepatitis C (HCV). During his workup for HCV treatment, the clinician orders a chest x-ray (CXR) due to the patient's complaint of a "cough that will not go away." The CXR reveals extensive bilateral cavitary lesions. The physician's office provides him with a surgical mask and notifies the local health department of a person with possible TB.

The patient is referred to the city health department where the TB public health nurse (PHN) conducts a nursing and social assessment revealing a history of alcohol use and untreated HCV. She notes that his current liver function tests (LFTs) are, ALT 150 units/L and AST 80 units/L. His housing situation is precarious, and he is currently sleeping on the sofa at his sister's trailer.

1.) What medical and/or social risk factors increase the patient's risk of hepatotoxicity while taking TB medications? (Circle all that apply.)

a. History of untreated HCV
b. Unstable housing
c. Veteran of the Armed Services
d. Alcohol use
e. Using over-the-counter (OTC) pain medication(s)

During the assessment at the health department, the PHN collects one sputum specimen due to the initial abnormal CXR consistent with TB. She provides the patient with containers to collect two additional specimens at least 8 hours apart, including one in the early morning.

> One sputum specimen should be collected during the initial clinic visit. Specimens should be obtained in an airborne infection isolation (AII) room, a sputum collection booth, or another isolated, well-ventilated area (e.g., outdoors).
>
> Patient education video for sputum collection: https://globaltb.njms.rutgers.edu/educationalmaterials/sputumcollectionvideo.php

The three sputa are 4+, 3+, 4+ AFB smear positive, and the Cepheid Xpert® (Xpert®) MTB/RIF results are positive for MTB complex and rifampin susceptible. Final cultures and susceptibilities are pending. His clinician, in consultation with a Center of Disease Control and Prevention (CDC) TB Center of Excellence physician, starts him on a liver friendly TB regimen due to his untreated HCV.

TB Treatment in a Patient at Risk of Hepatotoxicity

The PHN provides the patient with information about the early and late symptoms of hepatotoxicity. Typically, patients will have nausea and/or vomiting plus additional symptoms, recognizing that symptoms can overlap during the stages of hepatotoxicity. She also explains that alcohol and OTC pain medications, such as acetaminophen (Tylenol), can increase the chance of further liver damage. The patient understands the risks and agrees to try and limit both while on TB treatment. The PHN also provides resources about treatment for alcohol use. Utilizing a standardized agreement form helps him understand and document what actions to take to decrease his risk for further liver damage.

2.) Place a check mark in the column for either the early sign(s)/symptom(s) or later stage sign(s)/ symptom(s) of hepatotoxicity.

Hepatatoxicity Sign/Symptom	Early Sign(s)/Symptom(s) of Hepatatoxicity	Later Stage Sign(s)/Symptom(s) of Hepatatoxicity
Jaundice		
Fatigue		
Fever		
Loss of appetite		
Rash		
Abdominal pain/tenderness		
Nausea & vomiting		

Source: Curry International Tuberculosis Center (2018): *Nursing Guide for Managing Side Effects to Drug-resistant TB Treatment*, p. 20

TB treatment in patients with pre-existing advanced liver disease poses significant challenges. (Early and later symptoms are delineated in the chart's source as well as in the answer key found on page 40.) However, many times symptoms are not clear cut and may overlap between "early/late timeframes."

The PHN reviews the first-, second-, and third-line medications used for treating TB to determine which medications are more likely to cause hepatotoxicity.

3.) Match the medication(s) below with the description of their potential liver toxicity.

____	**Isoniazid (INH)**	**A.** This drug is **most** likely to cause hepatitis. In individuals with normal hepatic function, the hepatotoxic effects are usually reversible if the drug is stopped as soon as symptoms are evident. Hepatotoxicity appears to be increased when rifampin (RIF) is used.
____	**Rifampin (RIF)**	**B.** This drug has been indicated in hepatotoxic drug reactions.
____	**Pyrazinamide (PZA)**	**C.** This drug causes fewer episodes of hepatotoxicity than INH, but the events can be severe and prolonged, and worsen even after stopping therapy. This drug is thought to cause the most severe liver toxicity.
____	**Ethionamide (ETA)**	**D.** This drug more commonly causes a cholestatic jaundice but can potentiate the hepatocyte damage caused by INH.
____	**Fluroquinolones**	**E.** Some drugs in this class have been associated with occasional cases of liver damage.

Since the patient has co-morbid conditions and social factors, he will likely need intensive TB nurse case management for a successful treatment outcome. Due to his housing situation, the health department provides housing utilizing incentive funds to pay for a room in a single room occupancy (SRO) motel for potentially infectious persons with no or unstable housing. An SRO is a form of housing that does not share ventilation with other units and has a single outside entrance to decrease the chance of TB transmission. The health department also refers the patient to the Veterans Affairs (VA) for long term housing options.

> "Nurse case management, the use of incentives and enablers, and treatment administration by DOT have proven to be an effective triad to provide patient-centered care for safe and documented completion of TB."
>
> Source: http://www.tbcontrollers.org/resources/tb-infection/clinical-recommendations/

4.) Circle all that apply. Nurse case management activities include:

a. Providing daily DOT with assessment of adverse drug events
b. Assessing weight weekly until stable, then monthly
c. Measuring girth frequently, if abdominal distention is present
d. Assessing for TB symptoms weekly during the intensive phase, then monthly
e. Collecting sputa weekly until three consecutive smear negative; then monthly until two consecutive cultures are negative
f. Obtaining follow up CXRs and labs as ordered by clinician
g. All of the above

On home visit #10 for directly observed treatment (DOT), the PHN notes that the patient's eyes are jaundiced, and he complains of abdominal bloating and nausea.

5.) What are the next steps the PHN should take?

a. Do nothing, the patient has untreated HCV, so this is an expected reaction.
b. Hold ALL TB medications and draw blood for LFTs (per standing orders).
c. Give him his TB medications since he cannot start treatment for HCV until he is non-infectious.
d. None of the above

His laboratory results reveal a significant increase in the ALT (950 u/l) and AST (730 u/l). Per CDC recommendations, if any of the liver enzymes exceed three times the upper limit of normal with symptoms present or five times the upper limit of normal without symptoms, TB medications should be held. An ALT level ten times normal is severe toxicity.

The PHN holds all TB medications and notifies the treating clinician immediately. The patient is evaluated, and all TB medications are stopped. Although data to guide the monitoring of patients with pre-existing severe liver disease is scarce, based on his clinical condition and the clinician's

assessment, blood for LFTs and total bilirubin is drawn twice weekly until the LFTs return to less than two times the upper limit of normal and if elevated total bilirubin is <2.0 in accordance with the 2006 *Official American Thoracic Society (ATS) Statement: Hepatotoxicity of Antituberculosis Therapy*. For patients with an elevation of baseline liver enzymes, wait until return to near baseline levels of ALT (150 u/L) and AST (80 u/L) in accordance with the 2016 *ATS/CDC/Infectious Disease Society of America (IDSA) Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis*.

6.) Circle all that apply. Comfort measures and information the PHN provides may include:

a. Describing steps that can be taken to minimize side-effects as they occur
b. Instructing the patient to limit activity to conserve energy
c. Providing nutritional consultation by a registered dietitian to help ensure optimal food intake
d. Encouraging him to avoid alcohol
e. Explaining that he may feel worse before he feels better
f. All of the above

The treating clinician in consultation with a TB expert, begins a drug re-challenge by re-introducing one drug at a time to determine which drug is causing the increase in LFT values. The clinician will continue the drug re-challenge until the patient is receiving an effective TB regimen. The PHN closely assesses the patient for signs and symptoms of liver toxicity during the drug re-challenge, draws LFTs as ordered, and assures him that his symptoms will improve over time and that treatment will cure his TB disease.

The patient receives an extended treatment regimen with many stops and starts due to increased LFTs. After 12 months, he successfully completes TB treatment and begins treatment for HCV.

QUESTIONS AND ANSWERS

1.) What medical and/or social risk factors increase the patient's risk of hepatotoxicity while taking TB medications? (Circle all that apply.)

a. History of untreated HCV
b. Unstable housing
c. Veteran of the Armed Services
d. Alcohol use
e. Using over-the-counter (OTC) pain medication(s)

Rationale: Patients with advanced liver disease due to a variety of conditions, such as HCV, have a greater likelihood of drug-induced hepatitis during TB treatment. The implications of drug-induced hepatitis for patients with marginal hepatic reserve are potentially serious and life threatening. It is vital to educate and support patients with alcohol usage to minimize further damage to the liver. Utilizing a liver-friendly TB regimen is recommended in these situations. For patients with chronic pain, it is important to ensure they use pain medications that are not metabolized by the liver. Acetaminophen (Tylenol) is a common OTC that is potentially liver toxic. Offering the patient support for other methods of pain relief is important to minimize the potential for further liver damage.

2.) Place a check mark in the column for either the early sign(s)/symptom(s) or later stage sign(s)/symptom(s) of hepatotoxicity.

Hepatatoxicity Sign/Symptom	Early Sign(s)/Symptom(s) of Hepatatoxicity	Later Stage Sign(s)/Symptom(s) of Hepatatoxicity
Jaundice		X
Fatigue	X	
Fever		X
Loss of appetite	X	
Rash		X
Abdominal pain/tenderness	X	
Nausea & vomiting	X	

Source: Curry International Tuberculosis Center (2018): *Nursing Guide for Managing Side Effects to Drug-resistant TB Treatment*, p. 20. https://www.currytbcenter.ucsf.edu/products/nursing-guide-managing-side-effects-drug-resistant-tb-treatment

TB Treatment in a Patient at Risk of Hepatotoxicity

3.) Match the medication(s) below with the description of their potential liver toxicity.

B	**Isoniazid (INH)**	**A.** This drug is **most** likely to cause hepatitis. In individuals with normal hepatic function, the hepatotoxic effects are usually reversible if the drug is stopped as soon as symptoms are evident. Hepatotoxicity appears to be increased when rifampin (RIF) is used.
D	**Rifampin (RIF)**	**B.** This drug has been indicated in hepatotoxic drug reactions.
C	**Pyrazinamide (PZA)**	**C.** This drug causes fewer episodes of hepatotoxicity than INH, but the events can be severe and prolonged, and worsen even after stopping therapy. This drug is thought to cause the most severe liver toxicity.
A	**Ethionamide (ETA)**	**D.** This drug more commonly causes a cholestatic jaundice but can potentiate the hepatocyte damage caused by INH.
E	**Fluroquinolones**	**E.** Some drugs in this class have been associated with occasional cases of liver damage.

Rationale: Developing a liver friendly regimen for a patient with advanced liver disease can be challenging. Utilizing second- and third-line medications is oftentimes necessary. As the PHN, it is important to note that second- and third-line medications have a variety of side effects and to be aware of those during the nursing assessment. Utilize resources such as: *Nursing Guide for Managing Side Effects to Drug-resistant TB Treatment* (https://www.currytbcenter.ucsf.edu/products/nursing-guide-managing-side-effects-drug-resistant-tb-treatment) and *Drug Resistant Tuberculosis: A Survival Guide for Clinicians, 3rd Edition* (https://www.currytbcenter.ucsf.edu/products/view/drug-resistant-tuberculosis-survival-guide-clinicians-3rd-edition) chapter 5, p. 99 to aid in recognizing potential side effects and adverse events.

Source: Curry International Tuberculosis Center. *Drug Resistant Tuberculosis: A Survival Guide For Clinicians, 3rd edition*; p. 182. https://www.currytbcenter.ucsf.edu/products/view/drug-resistant-tuberculosis-survival-guide-clinicians-3rd-edition

4.) Circle all that apply. Nurse case management activities include:

a. Providing daily DOT with assessment of adverse drug events
b. Assessing weight weekly until stable, then monthly
c. Measuring girth frequently, if abdominal distention is present
d. Assessing for TB symptoms weekly during the intensive phase, then monthly
e. Collecting sputa weekly until three consecutive smear negative; then monthly until two consecutive cultures are negative
f. Obtaining follow up CXRs and labs as ordered by clinician
g. All of the above

Rationale: The daily interaction of the DOT worker and/or the PHN with the patient is often times the "lifeline" that keeps the patient adherent and able to successfully complete treatment. The assessments that the PHN provides are essential to detect any adverse events as early as possible to prevent negative long-term consequences for the patient.

5.) What are the next steps the PHN should take?

a. Do nothing, the patient has untreated HCV, so this is an expected reaction.
b. Hold ALL TB medications and draw blood for LFTs (per standing orders).
c. Give him his TB medications since he cannot start treatment for HCV until he is non-infectious.
d. None of the above

Rationale: Utilizing a standardized form to assess the patient at each visit for potential adverse drug events is essential. The patient may not recognize or acknowledge the subtle changes to their health, and it is essential that the PHN recognize them and promptly act. Even with untreated HCV, if the patient develops jaundice, it is important to stop the TB medications to not cause further liver damage. Some jurisdictions have standing orders to allow the nurse to draw blood immediately, other jurisdictions may require that the PHN contact the clinician for an order prior to drawing blood. Keep in mind, that some patients may have an overwhelming desire to complete TB treatment and may deny or minimize side effects related to TB medications.

In addition to elevation of ALT, disproportionate increases in bilirubin and alkaline phosphatase occasionally occur; these conditions are associated with RIF hepatotoxicity that should be evaluated promptly. If ALT levels are consistent with hepatotoxicity, drugs must be stopped. Drugs should also be stopped if total bilirubin is >2.0.

Source: *CDC Core Curriculum on Tuberculosis: What the Clinician Should Know*, p. 125. https://www.cdc.gov/tb/education/corecurr/index.htm

6.) Circle all that apply. Comfort measures and information the PHN provides may include:

a. Describing steps that can be taken to minimize side-effects as they occur
b. Instructing the patient to limit activity to conserve energy
c. Providing nutritional consultation by a registered dietitian to help ensure optimal food intake
d. Encouraging him to avoid alcohol
e. Explaining that he may feel worse before he feels better
f. All of the above

Rationale: The goal of TB nurse case managers is to provide patient-centered care for completion of treatment. It is important to build a trusting relationship with the patient and develop individualized plans to meet their specific needs. The PHN may provide connections to other partners, such as dietitians, drug/alcohol treatment programs, etc., to improve the patient's quality of life and ensure successful completion of treatment.

Case Study 5

Delayed Treatment Response

Delayed Treatment Response

Objectives:

- Describe methods for evaluating response to treatment.
- Identify indicators of a delayed response to tuberculosis (TB) treatment.
- List potential causes for a delayed treatment response.
- Outline patient-centered approaches for improving treatment adherence.

Case History:

A 50-year-old woman presented to her primary care provider (PCP) with a weight loss of 15 pounds, fever, cough, and hemoptysis. The PCP sent her to the emergency department (ED) at the local hospital, where her chest x-ray (CXR) report indicated multiple cavities. All three of her acid-fast bacilli (AFB) sputum smear results were 4+. A sputum sample was sent for nucleic acid amplification testing (NAAT) using Cepheid Xpert® (Xpert®) MTB/RIF; results indicated presence of *Mycobacterium tuberculosis* (*M. tuberculosis*) with no rifampin (RIF) resistance identified.

The patient was admitted to the hospital and placed on a four-drug regimen of RIF, isoniazid (INH), pyrazinamide (PZA), and ethambutol (EMB) for presumed drug-susceptible pulmonary TB. The specimen was sent for culture, drug-susceptibility testing (DST), and genotyping. After three weeks the isolate was reported to be susceptible to all first-line drugs, and EMB was discontinued. Her sputum smears converted to negative after four weeks of treatment.

By this point, the patient has been on treatment for eight weeks. The public health nurse (PHN) in a large rural county has been providing directly-observed therapy (DOT) since the patient's discharge from the hospital. Competing responsibilities and staff shortages have necessitated doing in-person DOT only twice-weekly, with the patient taking self-administered therapy (SAT) for the other three days.

At each DOT visit, the PHN:

- Observed the patient swallowing her pills,
- Assessed for signs and symptoms of TB and adverse effects,
- Gave the patient medications for the subsequent days where she would be self-administering, and
- Asked if she took the medications provided at the last visit.

The patient was pleasant and cooperative during DOT visits, and the PHN developed a good rapport with her. As part of the ongoing assessment activities, the PHN monitored the patient's response to treatment.

Clinical evaluation, bacteriological examination, and chest radiography are used to assess treatment response. The patient was evaluated by a clinician monthly during her treatment per established guidance (2016 Official American Thoracic Society/Centers for Disease Control and Prevention/ Infectious Diseases Society of America *Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis Guidelines*, p. 7) which included: vital signs, weight, TB symptoms, collection of sputum specimens, and any possible adverse effects from treatment.

Delayed Treatment Response

1.) Why is the monthly clinical evaluation important? (Circle all that apply.)

a. To assess adherence
b. To identify additional contacts
c. To identify possible adverse reactions to medications
d. To determine treatment efficacy

Sputum samples are collected from patients as needed during monthly monitoring visits for bacteriologic examination.

2.) When should future sputum samples be collected for this patient? (See table below for additional information.)

a. No further samples are needed since her sputum smears converted to negative after one month and culture results showed drug-susceptible TB.
b. Specimens should be collected at least monthly until two consecutive specimens are culture negative.
c. Specimens should be collected at least monthly until the Xpert® MTB/RIF results are negative for presence of *M. tuberculosis.*
d. Sputum should be collected monthly until the completion of treatment.

Bacteriologic Status	Recommendations for Response to Treatment
Positive sputum cultures before treatment	• Obtain specimens for culture at least monthly until 2 consecutive specimens are negative on culture • Obtain specimens for culture ast least monthly until 2 consecutive specimens are negative on culture • Perform monthly sputum AFB smears and cultures on MDR TB patients throughout entire treatment course • A repeat chest radiograph after 2 motnhs of treatment can be useful but is not essential

Negative sputum cultures before treatment	• Repeat chest radiograph at intervals based on clinical circumstances and differential diagnosis
	• If radiograph does not improve after patient has received 2 months of treatment, abnormality might be caused by
	  • Previous, not current, TB disease
	  • Another reason

Cultures have not converted to negative after 3 months of therapy	Re-evaluate for • Potential drug-resistant disease • Potential non-adherence to the regimen
Cultures are still positive after 4 months of treatment	Consider treatment to have failed and manage accordingly in consultation with an expert

Source: *CDC Core Curriculum on Tuberculosis: What the Clinician Should Know*, p. 127.
https://www.cdc.gov/tb/education/corecurr/index.htm

At the clinical monitoring visit after two months of treatment:

- The patient received a CXR.
- The PHN collected sputum and sent it for smear and culture.
- The PHN noted that the patient initially gained five pounds after one month of treatment; however, this month her weight remained stable.
- The patient did not report any symptoms of TB disease.

Delayed Treatment Response

When reviewing the CXR report, the PHN noted that the cavitation has not improved. During the next DOT visit, she noticed that the patient was coughing. The patient said she has had a cough for the last week or two and took some prescription cough syrup that she had on hand.

When the patient's AFB smear results came back, the PHN reviewed all of her bacteriological results, shown below:

Microbiologic results on samples collected after two months of treatment				
Sample Collection	**Smear**	**NAAT**	**Culture**	**DST**
Initial presentation (3 samples)	4+ x three specimens	Positive, no RIF resistance detected	+	Pan-susceptible
After 1 month of therapy	Negative	N/A	+	N/A
After 2 months of therapy	Positive	N/A	Pending	N/A

3.) What concerns should the PHN have about the patient's progress at this point?

a. Her smears initially converted to negative, but the samples collected at two months are AFB smear positive.
b. Her cough has recurred.
c. After an initial weight gain, her weight has leveled off.
d. Cavitation is still present on the CXR after 2 months of therapy.
e. All of the above

The PHN informed the treating physician of the patient's new cough and the most recent lab results.

4.) Which of the following could be potential causes for her clinical, bacteriologic, and radiographic findings?

Potential Cause	YES, NO, or N/A
Malabsorption of medications	
The over-the-counter ibuprofen she takes	
Poor adherence to treatment	
Development of drug-resistance	

Two weeks later, the PHN received results from the lab; the sample collected after two months of treatment grew *M. tuberculosis*. She is still culture positive after two months of treatment.

The treating physician ordered serum drug levels; results indicated that the patient had sub-therapeutic levels of RIF. The PHN requests a consult with a TB expert physician regarding the patient's RIF levels whereupon the physician recommends increased doses of RIF. The PHN also reviewed the patient's medical record and asked her about other medications to assess for other medical conditions or potential drug interactions that could affect serum drug levels. There were no evident findings which would impact RIF levels.

Delayed Treatment Response

Next, the PHN reviewed the patient's DOT log to identify any missed doses. She noted that in her biweekly visits to provide DOT for the first two and half months of treatment, the patient had only missed one visit, when she had to leave unexpectedly for a family emergency. She reported taking all the medication provided for self-administration. However, based on her response to treatment the PHN was concerned that she may not have taken those doses.

During the next DOT visit, the PHN tried to identify potential barriers to treatment adherence.

5.) What are some common potential barriers to treatment adherence?

a. Comorbidities
b. Side effects from the medications
c. Stigma
d. All of the above

The PHN discussed her concerns about the patient's delayed response to treatment and reiterated the need for adherence. She reminded the patient that not taking medications as prescribed can result in development of drug-resistance. When the PHN mentioned that sometimes people experience symptoms that make it difficult to take medications, she noticed that the patient hesitated before answering. As the PHN and the patient continued to talk, the patient mentioned that she had some diarrhea and nausea but was embarrassed to talk about it. She indicated that the red pills seemed to be the cause, and she sometimes didn't take those. She didn't tell the PHN because she didn't want to upset her or get into trouble. The PHN told the patient that she appreciated her honesty and suggested taking medications with food to minimize GI upset. The PHN also contacted the clinician who prescribed ondansetron (Zofran) for the patient's nausea.

eDOT

The option of eDOT, when available, is a patient-centered approach that can increase patient's autonomy and adherence to treatment. It should not be seen as a reward for treatment adherence but as a viable alternative.

The PHN discussed her concerns about the patient's treatment plan with her supervisor. Although DOT is an important tool to ensure adherence and is the standard of care for all patients with TB disease, resources do not allow for in-person visits for all of this patient's doses. The PHN and her supervisor decided to set up an electronic DOT (eDOT) program, following the protocols established by the state health department. The state policy was developed using the CDC resource *Implementing an Electronic Directly Observed Therapy (eDOT) Program: A Toolkit for Tuberculosis (TB) Programs*. The PHN discussed the plan for DOT with the patient and answered any questions. They select a time and place for eDOT, that takes the patient's preferences into account while ensuring patient privacy.

Therapeutic Drug Monitoring

Therapeutic drug levels can be important in clinical assessment of delayed response to TB treatment and allow for dose adjustments. However, programmatic funding and restraints may make them difficult to obtain.

Delayed Treatment Response

The patient continued the recommended regimen of daily treatment during the continuation phase of treatment. Two doses per week were provided in-person, and three were provided using eDOT.

At the next physician clinical visit, three months after initiation of therapy, the patient reported that her cough has resolved, and she has gained 5 pounds. However, she was still smear positive, and the cultures from the sample collected after three months of treatment came back positive. She was adherent to her in-person and electronic DOT.

6.) What additional tests should be considered at this point? (Circle all that apply.)

a. None
b. Repeat drug-susceptibility testing
c. LFTs

Serum drugs levels were repeated, and results came back within normal ranges.

> **Delayed Culture Conversion**
>
> A six-month treatment regimen is associated with a relapse rate of 20% in patients who have 1) cavitation and 2) a positive culture after two months of therapy. This compares to a 2% relapse rate in patients for six months who have neither factor. Thus, the continuation phase of treatment (INH and RIF) should be extended for an additional three months (total of nine months of treatment) in patients who have cavitation on the initial CXR and positive cultures at completion of two months of therapy. (2016 ATS/CDC/IDSA *Guidelines for Treatment of Drug-Susceptible TB,* p. 7).

Additional Information:

The patient continued to improve clinically and was adherent to her in-person and electronic DOT for the remainder of her treatment. Her nausea improved with the ondansetron. The sample collected after four months of treatment was smear and culture negative. The sample sent for repeat DST (after three months of treatment) did not indicate any drug resistance. She successfully completed treatment, which was extended to nine months of total therapy since she had cavitation on her initial X-ray and positive cultures after two months of therapy.

QUESTIONS AND ANSWERS

1.) Why is the monthly clinical evaluation important? (Select all that apply)

a. To assess adherence

b. To identify additional contacts

c. To identify possible adverse reactions to medications

d. To determine treatment efficacy

Rationale: Clinical evaluation, at least monthly, will help assess whether the patient is improving clinically and provides an opportunity to ask about adherence, review DOT logs, and assess for potential adverse effects. The patients progress and performance in these areas may impact the treatment plan, including regimen, medication administration, and length of treatment.

Source: *CDC Core Curriculum on Tuberculosis: What the Clinician Should Know*, p. 122. https://www.cdc.gov/tb/education/corecurr/index.htm

2.) When should future sputum samples be collected for this patient?

a. No further samples are needed since her sputum smears converted to negative after one month and culture results showed drug-susceptible TB.

b. Specimens should be collected at least monthly until two consecutive specimens are culture negative.

c. Specimens should be collected at least monthly until the Xpert® MTB/RIF results are negative for presence of *M. tuberculosis*.

d. Specimens should be collected monthly until the completion of treatment.

Rationale: Bacteriologic examination is part of assessing the patient's response to treatment. For patients with positive sputum cultures before treatment, specimens should be collected at least monthly until 2 consecutive specimens are negative on culture. Although NAATs like Xpert® MTB/RIF are important for initial confirmation of TB, the tests will also detect dead TB bacteria, and thus are not useful for monitoring the patient's response to therapy.

Source: *CDC Core Curriculum on Tuberculosis: What the Clinician Should Know*, p. 126-127. https://www.cdc.gov/tb/education/corecurr/index.htm

NTCA/APHL. (2016). *Consensus statement on the use of Cepheid Xpert MTB/RIF® assay in making decisions to discontinue airborne infection isolation in healthcare settings*, p. 5. http://www.tbcontrollers.org/docs/resources/NTCA_APHL_GeneXpert_Consensus_Statement_Final.pdf

Delayed Treatment Response

3.) What concerns should the PHN have about the patient's progress at this point?

a. Her smears initially converted to negative, but the samples collected at two months are AFB smear positive.
b. Her cough has recurred.
c. After an initial weight gain, her weight has leveled off.
d. Cavitation is still present on the CXR after 2 months of therapy.
e. All of the above

Rationale: During DOT and clinical visits, the PHN should identify and address potential barriers to treatment and closely monitor the patient's response to treatment. All of the above factors may indicate a delayed response to therapy. Though all patients respond to treatment at a different pace, all TB symptoms should gradually improve and eventually go away. Patients whose symptoms do not improve during the first two months of treatment, or whose symptoms worsen after improving initially should be investigated further to identify potential causes.

Source: *CDC Core Curriculum on Tuberculosis: What the Clinician Should Know*, p. 122. https://www.cdc.gov/tb/education/corecurr/index.htm

4.) Which of the following could be potential causes for her clinical, bacteriologic, and radiographic findings?

Potential Cause	YES, NO, or N/A
Malabsorption of medications	**YES**
The over-the-counter ibuprofen she takes	**NO**
Poor adherence to treatment	**YES**
Development of drug-resistance	**YES**

Rationale: If a patient's symptoms do not improve during the first two months of treatment, or if symptoms worsen after initial improvement, the patient should be evaluated for nonadherence, malabsorption (e.g., due to drug interactions, diabetes mellitus, or GI abnormalities), development of drug resistance, or symptoms consistent with immune reconstitution.

Source: *CDC Core Curriculum on Tuberculosis: What the Clinician Should Know*, p. 122. https://www.cdc.gov/tb/education/corecurr/index.htm

Delayed Treatment Response

5.) What are some common potential barriers to treatment adherence?

a. Comorbidities
b. Side effects from the medications
c. Stigma
d. All of the above

Rationale: There are many potential barriers to treatment adherence. Patients may have other medical conditions and may prioritize these over TB. Side effects such as nausea or fatigue can also contribute to non-adherence. There may be stigma and shame associated with a TB diagnosis which, along with personal and cultural health beliefs, can impact if and when a person will seek care, and their treatment. Stigma can also lead to feelings of isolation and depression, which can also impact treatment adherence. Other barriers include language, difficulty getting appointments, and limited time or financial resources to access appointments. Patients may also not fully understand their diagnosis and treatment, and the importance of treatment adherence. Utilizing a patient-centered approach including ongoing education at the appropriate level and providing opportunities for patients to express concern and ask questions can help address these barriers.

Source: ATS/CDC/IDSA. (2016). *Clinical Practice Guidelines: Treatment of Drug-Susceptible TB*, p. 2-3 & 15-16. https://www.cdc.gov/tb/publications/guidelines/pdf/Clin-Infect-Dis.-2016-Nahid-cid_ciw376.pdf

6.) What additional tests should be considered at this point? (Select all that apply.)

a. None
b. Repeat drug-susceptibility testing
c. LFTs

Rationale: Patients with drug-sensitive TB disease who remain culture positive after **three months** of treatment should have DSTs repeated. Resistance may have developed. If not already done, therapeutic drug monitoring can also be performed, as dose adjustments to TB may be needed due to sub-therapeutic drug levels.

Source: ATS/CDC/IDSA. (2016). *Clinical Practice Guidelines: Treatment of Drug-Susceptible TB*, p. 24 & 37. https://www.cdc.gov/tb/publications/guidelines/pdf/Clin-Infect-Dis.-2016-Nahid-cid_ciw376.pdf

Delayed Treatment Response

Notes:

Delayed Treatment Response

Notes:

Case Study 6

Culture Negative Tuberculosis

Culture Negative Tuberculosis

Objectives:

- Define diagnostic criteria for the diagnosis of culture negative tuberculosis (TB).
- Describe adequate treatment for culture negative TB.
- Describe what criteria is required for discontinuation of isolation.

Case History:

A 42-year-old diabetic male from a South Eastern Asian country with a high incidence of TB is referred to the local health department for a positive QuantiFERON TB test (QFT) that was performed by his primary care physician as a work requirement. He tells the public health nurse (PHN) "I need medical clearance as soon as possible because I'm not allowed to work without it." The PHN informed him of the medical clearance process and the need for further evaluation with a focused nursing assessment and a TB symptom screening.

The patient consents to further work-up, and during the nurse assessment, he shares that he immigrated to the United States two years ago, works in food service at a middle school and sends money home to support his family. He mentions his brother was treated for TB five years ago, but he himself has never been offered treatment. Furthermore, he verbalizes that his initial TB test that was required for entry into the country was positive, but he was told, "treatment was not needed."

1.) What factors put this patient at risk for TB disease?

a. He is a close contact to a person with infectious TB disease
b. He immigrated from an area of the world with high rates of TB
c. Having diabetes
d. All the above

He denies any current signs and symptoms of TB, but his physical assessment revealed a 10 pound weight loss over the course of two months. A chest x-ray (CXR) is ordered, and results noted "innumerable 1 to 2 mm nodular foci and scant infiltrates throughout the bilateral lung fields."

2.) Which of the following explanations by the nurse to the patient is most accurate?

a. You do not have signs and symptoms of TB, so no further action is needed.
b. You have no TB symptoms, your CXR is not consistent with TB, you are not contagious, but you may need further evaluation.
c. I will provide you with a surgical mask and ask that you remain at home and limit your interactions to household members only until further evaluation.
d. I will provide you with an N-95 respirator and ask that you remain at home and limit your interactions to household members only until further evaluation.

The patient was placed on home isolation and three consecutive sputum samples were collected at eight-hour intervals. The sputum samples were sent for acid-fast bacilli (AFB) smear, Nucleic Acid Amplification Test (NAAT), and culture. Sputum results were all AFB smear negative with cultures pending; NAAT was negative.

3.) What should you anticipate regarding the infectiousness for this patient?

a. He does not have TB disease and can be cleared for work. No further evaluation is required.
b. He has had three consecutive negative AFB smears and a negative NAAT; infectiousness is unlikely.
c. He must remain on airborne isolation until AFB cultures are negative on all three samples.
d. None of the above

Understanding that negative AFB smears and a negative NAAT does not exclude a diagnosis of active TB, and considering that the patient is at high risk for active TB disease due to his country of origin, his recent weight loss, and the abnormal CXR, the physician chooses the diagnosis of presumed pulmonary tuberculosis. The following baseline work-up is ordered: CBC, CMP, HIV, HGB A1C, Ishihara and Snellen exam. The physician also prescribes rifampin, isoniazid, pyrazinamide, and ethambutol (RIPE) based on the patient's weight.

The PHN understands that patients who, based on careful clinical and radiographic evaluation are thought to have pulmonary tuberculosis, should have treatment initiated with RIPE until all specimens collected return with results. The PHN provides education regarding needed evaluations and reassures the patient that results will be communicated as soon as they become available.

Nine weeks into treatment, all AFB smears and culture results are negative. A repeat CXR is ordered for this patient with comparison to baseline imaging and an office visit is scheduled to discuss his radiology results and evaluate the patient clinically. The PHN receives the following radiographic impression:

CXR with comparison to baseline study: Resolution of infiltrates in bilateral lung fields.

The follow up clinical assessment reveals: 8 pound weight gain. Subjectively, the patient states he "feels great" and denies any intolerance to the TB medications, and based on his physical assessment, the physician decides to continue TB meds (RIPE). The patient verbalizes that he does not understand why he needs to continue TB treatment if "his tests" are negative.

4.) What responses to treatment did this patient have?

a. Patient has gained weight and feels great.
b. Resolution of infiltrates on imaging and an 8 pound weight gain after 2 months of TB treatment.
c. He has not had significant improvement while on treatment. His CXR still shows abnormalities.
d. None of the above

The patient understands that he has improved while taking his TB medication. He consents to continuing therapy but wonders why he must take so many medications.

The PHN shares the patient's concern with the physician, and she states that after reviewing his medical record and determining: all cultures on adequate samples were negative and there is clinical and radiographic response after 2 months of intensive phase therapy, the continuation phase can continue with isoniazid and rifampin and subsequently be shortened to 2 months. The patient will need a total of 4 months of DOT to complete adequate treatment.

> All four drugs should be used for culture negative TB as a safequard against possible undetected drug resistance. If the source case is known and the isolate is drug susceptible, EMB can be stopped after the initial two months. If possible, PZA should be continued for all four months.

You share the news with the patient, and he continues to complete 4 months total treatment for culture negative pulmonary TB. The PHN sends him for an end of treatment CXR with comparison and receives the following results:

Lungs clear, complete resolution of bilateral infiltrates, and nodules no longer seen.

The PHN explains to the patient that after careful clinical evaluation his doctor has determined him cured of TB, and a Certificate of Treatment Completion is given to the patient.

Additional Information:

The diagnosis and treatment of culture negative TB will decrease the development of highly transmissible disease and reduce the need for contact investigation.

QUESTIONS AND ANSWERS

1.) What factors put this patient at risk for TB disease?

a. He is a close contact to a person with infectious TB disease
b. He immigrated from an area of the world with high rates of TB
c. Having diabetes
d. All of the above

Rationale: This person has three of the most common risk factors of having TB or developing TB from LTBI. He is from a country with a high incidence of TB, Thailand is one of the 30 world high TB burden countries. He was in contact to his brother who was diagnosed with TB 5 years prior and having diabetes is a comorbidity that prompts this patient at high risk to develop TB disease due to his weakened immune system. Having diabetes triples the risk of TB.

Source:

World Health Organization, South-East Asia. (2023). *Co-morbidities-TB*. https://www.who.int/southeastasia/activities/co-morbidities-tb

Centers for Disease Control and Prevention. (2016, March 18). *TB Risk Factors.* https://www.cdc.gov/tb/topic/basics/risk.htm

2.) Which of the following explanations by the nurse to the patient is most accurate?

a. You do not have signs and symptoms of TB, so no further action is needed.
b. You have no TB symptoms, your CXR is not consistent with TB, you are not contagious, but you may need further evaluation.
c. I will provide you with a surgical mask and ask that you remain at home and limit your interactions to household members only until further evaluation.
d. I will provide you with an N-95 respirator and ask that you remain at home and limit your interactions to household members only until further evaluation.

Rationale: Patients with a CXR suggestive of active TB as in this case reporting "infiltrates throughout the bilateral lung fields" should be promptly placed in isolation until negative sputum samples are obtained.

Source: Radiological Society of North America. (2017, January 11). *Pulmonary TB: Role of Radiology in Diagnosis and Management.* https://pubs.rsna.org/doi/full/10.1148/rg.2017160032

3.) What should you anticipate regarding the infectiousness for this patient?

a. He does not have TB disease and can be cleared for work. No further evaluation is required.
b. He has had three consecutive negative AFB smears and a negative NAAT; infectiousness is unlikely.
c. He must remain on airborne isolation until AFB cultures are negative on all three samples.
d. None of the above

Rationale: Patients with three consecutive negative AFB smears, and negative NAAT are unlikely to be infectious and do not need isolation.

Source: Heartland National TB Center. (2019). *Guidance on Release from Hospital Tuberculosis Isolation*. https://www.heartlandntbc.org/wp-content/uploads/2021/12/guidelines_home_hospital_infectious_patients.pdf

Centers for Disease Control and Prevention. *Controlling Tuberculosis in the United States*. MMWR: November 4, 2005; Volume 54 (RR12s). https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5412a1.htm

4.) What responses to treatment did this patient have?

a. Patient has gained weight and feels great.
b. Resolution of infiltrates on imaging and had a 8-pound weight gain after 2 months of TB treatment.
c. He had not had significant improvement on treatment. His CXR still shows abnormalities.
d. A & B

Rationale: "Patients who have negative cultures but who are presumed to have pulmonary tuberculosis should have thorough clinical and radiographic follow-up after 2–3 months of therapy. If there is clinical or radiographic improvement and no other problem is identified, TB treatment should be continued."

Source: Heartland National TB Center and Mayo Clinic. (2020). *The Spectrum of Tuberculosis from Infection to Disease, TB at a Glance, 3rd Edition.* https://www.heartlandntbc.org/assets/products/The_Spectrum_of_TB.pdf

Notes:

Case Study 7

Pediatric Tuberculosis

Pediatric Tuberculosis

Objectives:

- List the two types of tuberculosis (TB) tests used to diagnose TB infection in children.
- List the treatment regimens for TB disease for children.
- Describe methods to facilitate ingestion of TB medications in children.

Case History:

A four-year-old boy was taken for a routine well-child check up by his mother in preparation for him to start school in the fall. The child lives in a remote area of New Mexico with his mother, father, and several extended family members.

Table 1. Questions for Determining Risk of TB Infection in Children in the United States
• Has a family member or contact had tuberculosis disease?
• Has a family member had a positive tuberculin skin test result?
• Was your child born in a high-risk country (countries other than the United States, Canada, Australia, New Zealand, or Western and North European countries)?
• Has your child traveled to a high-risk country? If so, how much contact did your child have with the resident population?

During the well-child visit, the pediatrician performed a pediatric TB risk assessment utilizing the questions in the following table.

The child's mother answered "no" to all the questions and stated that her husband's brother used to visit frequently and now lives with them. She also stated that he is a heavy smoker, has a terrible cough, recalls him mentioning something about TB, and that he was treated for "walking pneumonia" recently.

1.) Based on the child evaluation and the information provided by the mother, should the pediatrician perform a TB test?

a. Yes
b. No

The pediatrician explains to the mother that there are two types of tests that can be utilized to detect Mycobacterium tuberculosis (*M. tuberculosis*); the Mantoux TB Skin Test (TST) and the Interferon Gamma Release Assay (IGRA) blood test.

2.) Which is the best TB test to utilize for a 4-year-old child?

a. IGRA
b. Mantoux TST
c. Either TST or IGRA can be used
d. No TB test is indicated at this time

The mother preferred for a TB skin test to be placed so the pediatrician alerted the public health department who placed a TB skin test on the child. Arrangements were made for the public health nurse (PHN) to do a home visit to read the TST in 72 hours.

In preparation for the home visit, the PHN took some sputum containers to collect sputum on the child's uncle since he has a prolonged cough and history of pneumonia.

During the home visit the PHN read the child's TST as positive at 11 mm induration. Since an induration of 11 mm is considered positive in children younger than 5 years of age or who have been exposed to adults in high-risk categories, radiographic evaluation is needed to evaluate for active TB disease.

TST Interpretation

Induration ≥ 5 mm considered positive in:	Induration ≥ 10 mm considered positive in:	Induration ≥ 15 mm considered positive in:
HIV infected individuals	Immigrants from high-prevalence countries	Any person, including persons with no known risk factors for TB. **Note:** Targeted skin testing programs should only be conducted among high-risk groups.
A recent contact of a person with TB disease	Persons with clinical conditions that place them at high risk	
Persons with fibrotic changes of CXR consistent with prior TB	Residents and employees of high-risk congregate settings	
Patients with organ transplants	Mycobacteriology laboratory personnel	
Individuals immunocompromised for other reasons (e.g. taking TNF-alpha inhibitors, taking equivalent of ≥15 mg/day of prednisone for ≥ 1 month)	Infants, children, and adolescents exposed to adults in high-risk categories	
	Children < 5 years old	
	Injection drug users	

Heartland National TB Center and Mayo Clinic, 2020: *The Spectrum of Tuberculosis from Infection to Disease, TB at a Glance, 3rd Edition*. Table 1.

3.) What is the next step for the PHN to take?

a. Have the child's mother schedule a follow-up appointment with his primary care pediatrician who ordered he TST.
b. Review the signs and symptoms of active TB with the child's mother and only do a chest x-ray (CXR) if he develops a cough.
c. Assist the child's mother with making arrangements to have a CXR done later that day.
d. No follow-up is needed.

The child's mother promptly takes him for a CXR; it revealed a finding of hilar lymphadenopathy. The pediatrician diagnosed the child with TB disease.

4.) Is this child considered infectious?

a. Yes
b. No

> "A diagnosis of TB nfection or TB disease in a young child is a public health sentinel event often representing recent transmission."

During a follow-up home visit, the PHN played a "coughing game" with the child outside and was able to collect a sputum specimen to send to the TB lab for acid-fast bacilli (AFB) smear, culture, Nucleic Acid Amplification Test (NAAT), and drug-susceptibility testing (DST).

The state TB laboratory notified the health department that the child's uncle is 4+ sputum smear positive, NAAT positive and the culture is pending. However, the child's sputum specimen is smear and NAAT negative. The child was initiated on TB treatment with two months of rifampin (RIF), isoniazid (INH), pyrazinamide (PZA) and ethambutol (EMB) daily by directly observed therapy (DOT) to be followed by four months of INH and RIF.

The health department works with the child's family to find alternate housing for the uncle since he is very infectious. The mother tells the PHN that she prefers to give her son his daily TB medications rather than her drive out every day to their home.

5.) What should be the PHN's response?

a. Agree with the mother that she can provide the TB medications for her son.
b. Explain to the mother that it is the standard of care to provide DOT for all persons with active TB.
c. Tell the mother that once the child finishes the first two months of treatment she can take over TB medication administration.
d. Discuss the best time for the mother to return to the clinic for DOT.

The PHN provides the child his TB medications daily by DOT, in his home. Upon arrival, the PHN crushed the INH, PZA, and EMB and opened the RIF capsule. The child was fussy about taking all the TB medications.

Patient Centered Care:
When TB medications are administered to a child, try to make the process pleasant, effective and friendly for the child.

6.) What should the PHN have done to aid in the administration of the medicine?

a. Mix the TB medications with jelly, applesauce, peanut butter, or marshmallow cream
b. Provide the child with a prize like stickers or toys.
c. Try to administer the medications the next visit
d. A & B

The PHN provided a variety of tasty treats to mix with the medications and also provided small prizes to the child when he took the medications each day.

Additional Information:

It is essential to do a source case investigation, starting with the parents, to determine who may have transmitted TB to the child. Transmission of *M. tuberculosis* complex is airborne, with inhalation of droplet nuclei usually produced by an adult or adolescent with contagious pulmonary, endobronchial, or laryngeal TB disease.

The probability of transmission increases if the index person has a positive acid-fast sputum smear, productive cough, or pulmonary cavities or is a household contact. It can be a complicated and time-consuming but very necessary process to determine who is the source person.

> Because the child lives with several extended family members, the child's parents and other adults living in the home should be included in the source case investigation.

Evaluation of a child that is a contact to a high-risk adult is a priority regardless of the presence of symptoms. The TB screening should include a medical evaluation, TST or IGRA, and CXR.

It is important to initiate TB treatment promptly by DOT when active TB is suspected.

Using tips and tricks as strategies to administer medication will aid in completing treatment successfully. In this situation the PHN found a strategy to successfully administer and complete six months of treatment.

An independent contact investigation will also be done related to the uncle since he was diagnosed with infectious TB disease.

QUESTIONS AND ANSWERS

1.) Based on the child evaluation and the information provided by the mother, should the pediatrician perform a TB test?

a. Yes

b. No

Rationale: Despite the mother answering "no" to all the questions from the pediatric risk assessment (Table 1), the patient's mother indicated that there was a person living in the household who had signs and symptoms of active TB disease; that would make the uncle a high-risk adult, therefore a TST or IGRA should be done. Also, it is not uncommon for individuals to have a diagnosis of pneumonia prior to receiving an accurate diagnosis of TB.

Source: *Red Book Online | Section 3 – Summaries of Infectious Diseases, Tuberculosis Chapter Updates: November 28, 2022*; 32

2.) Which is the best TB test to utilize for a 4-year-old child?

a. IGRA

b. Mantoux TST

c. Either TST or IGRA can be used

d. No TB test is indicated at this time

Rationale: The Red Book indicates for children 2 years and older, either TST or IGRA can be used, but in people previously vaccinated with bacilli-calmette Guerin (BCG), IGRA is preferred to avoid a false-positive TST result caused by a previous vaccination with BCG. Since the child had not received a BCG vaccination, placing a TST was an acceptable strategy The published experience testing children with IGRAs demonstrates that IGRAs consistently perform well in children 2 years and older, and some data support their use for even younger children.

Source: *Red Book Online | Section 3 – Summaries of Infectious Diseases, Tuberculosis Chapter Updates: November 28, 2022*; 38

3.) What is the next step for the PHN to take?

a. Have the child's mother schedule a follow-up appointment with his primary care pediatrician who ordered the TST.

b. Review the signs and symptoms of active TB with the child's mother and only do a CXR if he develops a cough.

c. Assist the child's mother with making arrangements to have a CXR done later that day.

d. No follow-up is needed.

Rationale: Although both IGRA and TST provide evidence for infection with *M. tuberculosis*, they cannot distinguish TB infection from TB disease. Patients testing positive for *M. tuberculosis* by IGRA or TST should be assessed for TB disease before initiating any therapeutic intervention. This assessment should include: (1) asking about symptoms of TB disease and exposure to TB patients; (2) physical examination for signs of TB disease; and (3) a chest radiograph. If radiographic signs of

TB (eg, airspace opacities, pleural effusions, cavities, or changes on serial radiographs) are seen, then sputum or gastric aspirate sampling should then be performed.

Source: *Red Book Online | Section 3 – Summaries of Infectious Diseases, Tuberculosis Chapter Updates: November 28, 2022*; 12

4.) Is this child considered infectious?

a. Yes
b. No

Rationale: Children younger than 10 with only adenopathy in the chest or small pulmonary lesions (paucibacillary disease) and non-productive cough are not contagious.

Source: *Red Book Online | Section 3 – Summaries of Infectious Diseases, Tuberculosis Chapter Updates: November 28, 2022;* 6

5.) What should be the PHN's response?

a. Agree with the mother that she can provide the TB medications for her son.
b. Explain to the mother that it is the standard of care to provide DOT for all persons with active TB.
c. Tell the mother that once the child finishes the first two months of treatment she can take over TB medication administration.
d. Discuss the best time for the mother to return to the clinic for DOT.

Rationale: The major problem limiting successful treatment is poor adherence to prescribed treatment regimens. The use of DOT decreases the rates of relapse, treatment failures, and drug resistance; DOT is strongly recommended by the Red Book and is program policy for many TB programs around the country for treatment of all persons, including children, with TB disease.

Source: *Red Book Online | Section 3 – Summaries of Infectious Diseases, Tuberculosis Chapter Updates: November 28, 2022;* 18

6.) What should the PHN have done to aid in the administration of the medicine?

a. Mix the TB medications with jelly, applesauce, peanut butter, or marshmallow cream.
b. Provide the child with a prize like stickers or toys.
c. Try to administer the medications the next visit.
d. A & B

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

Source: Heartland National TB Center. (2021). *Treatment Regimens and Dosing Recommendations for Treating Children with LTBI (Including Window Prophylaxis)*. Retrieved from https://www.heartlandntbc.org/wp-content/uploads/2021/12/tip_for_treating_LTBI_in_children.pdf

Notes:

Notes:

Case Study 8

Patient with Multi-Drug Resistant TB

Patient with Multi-Drug Resistant TB

Objectives:

- Identify the challenges in diagnosing, treating, and managing multi-drug resistant TB (MDR-TB) to include comorbid conditions such as diabetes mellitus.
- Identify risk factors for developing MDR-TB.
- Discuss minimum baseline test needed to start treatment for MDR-TB, screening tests required during treatment, and the importance of the monitoring process.
- Identify the most common side effects of specific second line medications and their management.

Case History:

A 33-year-old Asian female refugee presented to the emergency department (ED) at the University Hospital with cough, hemoptysis, fever, chills, night sweats, fatigue, and weight loss. Her chest x-ray (CXR) showed bilateral reticulonodular opacities and cavitation in the right upper lobe. She and her husband immigrated to the United States 4 years ago. She speaks little English, but with the assistance of a translator she verbalized that she is a housewife, her husband was a schoolteacher in Myanmar, and she remembered that as a teenager she was treated for TB "on and off" for almost a year. She could not recall any details about the types of medications, their names, or the number of specific pills. She did not remember receiving any injections. She denied any additional medical problems.

Due to her TB risk factors and clinical and radiographic presentation she was admitted with a diagnosis of pulmonary tuberculosis and placed in a respiratory isolation room. TB evaluation included sputum smear for acid fast bacilli (AFB) and culture, Cepheid GeneXpert® (Xpert®) MTB/RIF assay and a QuantiFERON Gold In-Tube Assay® (QFT).

1.) Does her previous TB treatment impact her current treatment plan?

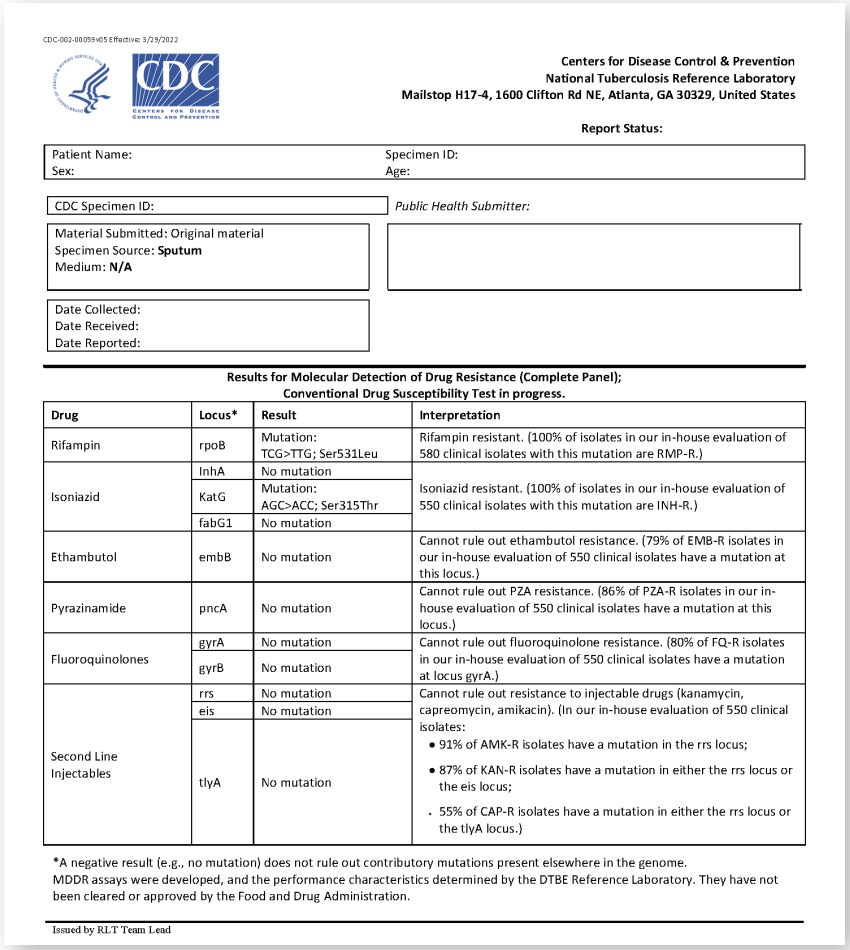
a. Yes; she is from a high burden country and could have MDR-TB
b. No; she does not have documentation of treatment
c. Yes; she recalls taking medication "on and off for almost a year"
d. A & C

Results:

- QFT positive.
- HIV negative. Pregnancy test negative. CBC and CMP were unremarkable.
- Sputum specimens were reported as AFB smear positive.
- Baseline labs were significant for A1C of 7.8 %; she was newly diagnosed with diabetes and the physician prescribed diabetes treatment.

The Gene Xpert, a rapid molecular assay for detection of MTB DNA in a clinical specimen and if MTB is present for evidence of possible rifampin resistance, was reported "likely rifampin resistant (RR)." The sample was sent to the Centers for Disease Control and Prevention (CDC) for MDDR (Molecular Detection of Drug Resistance), and five days later the preliminary report showed:

Patient with Multi-Drug Resistant TB



CDC-002-00059v05 Effective: 3/29/2022

Centers for Disease Control & Prevention
National Tuberculosis Reference Laboratory
Mailstop H17-4, 1600 Clifton Rd NE, Atlanta, GA 30329, United States

Report Status:

Patient Name:	Specimen ID:
Sex:	Age:

CDC Specimen ID:

Public Health Submitter:

Material Submitted: Original material
Specimen Source: **Sputum**
Medium: **N/A**

Date Collected:
Date Received:
Date Reported:

Results for Molecular Detection of Drug Resistance (Complete Panel); Conventional Drug Susceptibility Test in progress.

Drug	Locus*	Result	Interpretation
Rifampin	rpoB	Mutation: TCG>TTG; Ser531Leu	Rifampin resistant. (100% of isolates in our in-house evaluation of 580 clinical isolates with this mutation are RMP-R.)
Isoniazid	InhA	No mutation	Isoniazid resistant. (100% of isolates in our in-house evaluation of 550 clinical isolates with this mutation are INH-R.)
	KatG	Mutation: AGC>ACC; Ser315Thr	
	fabG1	No mutation	
Ethambutol	embB	No mutation	Cannot rule out ethambutol resistance. (79% of EMB-R isolates in our in-house evaluation of 550 clinical isolates have a mutation at this locus.)
Pyrazinamide	pncA	No mutation	Cannot rule out PZA resistance. (86% of PZA-R isolates in our in-house evaluation of 550 clinical isolates have a mutation at this locus.)
Fluoroquinolones	gyrA	No mutation	Cannot rule out fluoroquinolone resistance. (80% of FQ-R isolates in our in-house evaluation of 550 clinical isolates have a mutation at locus gyrA.)
	gyrB	No mutation	
Second Line Injectables	rrs	No mutation	Cannot rule out resistance to injectable drugs (kanamycin, capreomycin, amikacin). (In our in-house evaluation of 550 clinical isolates: • 91% of AMK-R isolates have a mutation in the rrs locus; • 87% of KAN-R isolates have a mutation in either the rrs locus or the eis locus; • 55% of CAP-R isolates have a mutation in either the rrs locus or the tlyA locus.)
	eis	No mutation	
	tlyA	No mutation	

*A negative result (e.g., no mutation) does not rule out contributory mutations present elsewhere in the genome.
MDDR assays were developed, and the performance characteristics determined by the DTBE Reference Laboratory. They have not been cleared or approved by the Food and Drug Administration.

Issued by RLT Team Lead

2.) Based on the results from the MDDR report above, what can be concluded?

a. The patient has disseminated MDR-TB
b. There is an rpoB mutation that is consistent with rifampin resistance (RR)
c. The katG mutation is consistent with high level INH resistance
d. All of the above

The patient was placed in respiratory isolation, she received fluids and medications to control fever and chills, and she remained stable. Due to the diagnosis of MDR-TB, expert medical consultation was requested.

The medical consultant recommended additional medical evaluation and laboratory tests and suggested the new shorter course all oral treatment recommended by the World Health Organization (WHO) if no contra-indications identified during the additional testing.

This regimen, bedaquiline, pretomanid, linezolid and moxifloxacin (BPaL + Moxifloxacin or BPaLM), is administered daily by directly observed therapy (DOT) for a duration of 26 weeks. The medical consultant also recommended monthly monitoring of side effects. Prior to initiating TB treatment, the hospital case manager utilized a translator to provide the patient with TB education and educational materials in her language; she was educated about side effects, length of treatment, and the importance of DOT. She was also educated about diabetes and was provided with educational materials about diet.

The patient had no identified contra-indications to BPaLM, and treatment was started with the following:

- Bedaquiline 400 mg daily for **2 weeks** then 200 mg 3x/week for 24 weeks
- Pretomanid 200 mg daily x 26 weeks
- Linezolid 600 mg daily x 26 weeks
- Moxifloxacin 400 mg x 26 weeks

Once the local public health team completed the initial contact investigation interview and determined that there were no individuals at high risk for progressing to active TB, if infected and living in her home, she was discharged from the hospital. Outpatient MDR-TB treatment was continued by the public health department and was tolerated well. The patient's nurse case manager provided the patient and her husband with educational material in her language and utilized the language line to communicate throughout the duration of TB treatment. Screening for TB in the patient's husband and other close contacts was initiated after the initial contact investigation interview conducted in the hospital.

After one month of MDR-TB treatment, the patient's sputum smears converted to negative and at two months the laboratory reported the first negative culture. TB symptoms resolved, and her monthly toxicity monitoring assessments were normal. The patient was in good spirits and had expressed interest in taking college courses and learning English. The PHN used a community resource directory to provide resources related to refugee support services; she enrolled in English as a Second Language (ESL) and college classes.

> Enrolling patient in ESL classes as well as other social support groups promotes patient well-being and allows the patient to gain confidence in communicating with others. It also creates a treatment partnership with the health department and improves communication.

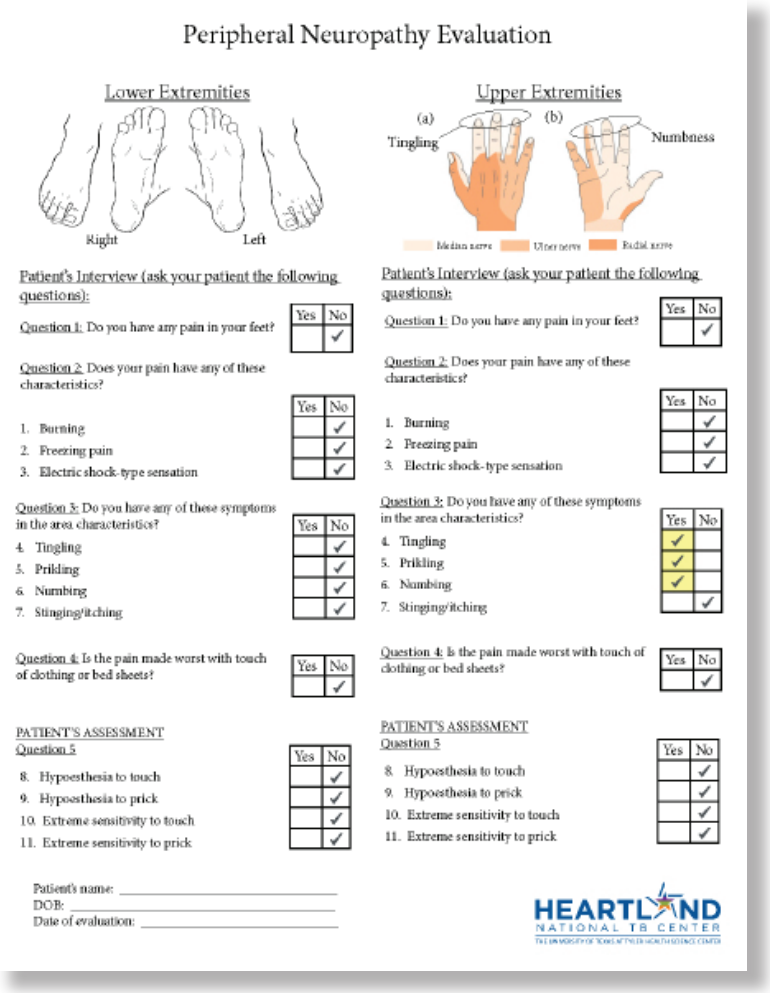
The patient appeared to be doing well, she started practicing her English during DOT visits. During the fourth month of treatment, she started having complaints of mild numbness and tingling in her hands.

3.) Which condition or medication in her MDR-TB treatment might be attributing to symptoms that suggest development of peripheral neuropathy (PN)?

a. It could be a side effect of linezolid
b. It could be a side effect of bedaquiline
c. It could be related to her diabetes
d. A & C

The evaluation revealed mild PN in the patient's hands. (See the Peripheral Neuropathy Evaluation found on page 75.)

Patient with Multi-Drug Resistant TB



Peripheral Neuropathy Evaluation

Lower Extremities

Right Left

Upper Extremities

(a) Tingling (b) Numbness

Median nerve Ulnar nerve Radial nerve

Patient's Interview (ask your patient the following questions):

Question 1: Do you have any pain in your feet? Yes ☐ No ☑

Question 2: Does your pain have any of these characteristics?

1. Burning — No ☑
2. Freezing pain — No ☑
3. Electric shock-type sensation — No ☑

Question 3: Do you have any of these symptoms in the area characteristics?

4. Tingling — No ☑
5. Prikling — No ☑
6. Numbing — No ☑
7. Stinging/itching — No ☑

Question 4: Is the pain made worst with touch of clothing or bed sheets? No ☑

PATIENT'S ASSESSMENT

Question 5

8. Hypoesthesia to touch — No ☑
9. Hypoesthesia to prick — No ☑
10. Extreme sensitivity to touch — No ☑
11. Extreme sensitivity to prick — No ☑

Patient's name: _____

DOB: _____

Date of evaluation: _____

Patient's Interview (ask your patient the following questions):

Question 1: Do you have any pain in your feet? Yes ☐ No ☑

Question 2: Does your pain have any of these characteristics?

1. Burning — No ☑
2. Freezing pain — No ☑
3. Electric shock-type sensation — No ☑

Question 3: Do you have any of these symptoms in the area characteristics?

4. Tingling — Yes ☑
5. Prikling — Yes ☑
6. Numbing — Yes ☑
7. Stinging/itching — No ☑

Question 4: Is the pain made worst with touch of clothing or bed sheets? No ☑

PATIENT'S ASSESSMENT

Question 5

8. Hypoesthesia to touch — No ☑
9. Hypoesthesia to prick — No ☑
10. Extreme sensitivity to touch — No ☑
11. Extreme sensitivity to prick — No ☑

HEARTLAND NATIONAL TB CENTER

The PHN asked the patient about her diabetes treatment, and she stated that she had not filled her prescription for the diabetes medication because she didn't have insurance. Further discussion with the patient revealed that she was not adherent with a diabetic diet.

Recommendations were given to monitor linezolid serum levels to include peak level at 2 hours and trough level right before the next dose. Repeat labs were drawn and compared to baseline labs, the HbA1C was 8.9%. Diabetes was suspected to be contributing, if not the sole cause of the newly identified symptoms of neuropathy. She was referred to a community clinic where she was enrolled in the diabetes program and started on Metformin. Serum level results were: trough linezolid concentration was 1.2 mcg/mL, and the peak concentration level was 15.9 mcg/mL.

> Patient-centered case management helps patients understand their diagnosis, participate in their treatment, and discuss potential barriers to treatment.
>
> *WHO Guidelines for the programmatic management of drug resistant TB Companion*

4.) How do you interpret these results??

a. Abnormal value: Linezolid trough concentration level is too high
b. Abnormal value: Linezolid peak concentration level is too high
c. Both levels are in the normal range
d. Abnormal value: Peak level is too low

The provider decided to continue linezolid with enhanced monitoring of peripheral neuropathy. A normal trough is helpful in lessening the likelihood of linezolid associated toxicity, including peripheral neuropathy, but does not eliminate this possibility. It is reasonable to observe carefully for improvement with control of diabetes. The provider planned that if symptoms of neuropathy progressed, linezolid would be held. Three weeks later, the PN improved, and the patient continued with the treatment regimen of bedaquiline 200 mg on Monday, Wednesday, and Friday, and moxifloxacin, pretomanid, and linezolid daily.

During the following toxicity monitoring visit, the case manager found the patient complains of palpitations and anxiety. A mental health assessment was completed, and the PHN inquired about her current personal situation. The results of the mental health assessment indicated a mild change from baseline but no signs of depression.

5.) Which medication in her MDR-TB treatment regimen might have attributed to her palpitations and anxiety?

a. Linezolid
b. Moxifloxacin
c. Bedaquiline
d. B & C

The treatment regimen was reviewed, and the provider noted that both bedaquiline and moxifloxacin could cause QTc prolongation that may lead to arrythmias. An EKG was taken, and the QTc was 445ms with a normal sinus rhythm.

6.) Is the QTc result normal or abnormal for a female patient?

a. Normal
b. Abnormal

Because the patient had no EKG evidence of an abnormal heart rhythm but was experiencing a sensation of palpitations, the nurse case manager interviewed her for any other possible causes. The patient shared with the nurse that she was having anxiety due to personal problems that caused stress in her life. Her father who still lived in Southeast Asia was diagnosed with a terminal disease, and she verbalized that she has been drinking too much caffeine. The patient was educated to limit or omit (if possible) her caffeine intake and encouraged to exercise and relax. She was encouraged to talk about the struggles with being separated from a loved one who is seriously ill and (if needed) ask for help in finding a counselor.

Follow up CXR's at six months showed marked improvement when compared to the baseline CXR with resolution of cavities and minimal remaining opacities. The HbA1c decreased to 7.2%. She successfully completed 26 total weeks of treatment. Her case management team planned a small party and celebrated her cure with her husband.

Additional Information

MDR-TB treatment may be challenging for your patient; therefore, it is imperative to identify and address barriers to treatment and involve the patient in decision making as much as possible in elements of their care. By eliminating barriers and giving patient-centered care, treatment can be less challenging for the patient and can lead to successful completion of MDR-TB treatment.

Patient with Multi-Drug Resistant TB

Links

1. **Burma TB Roadmap overview** https://www.usaid.gov/sites/default/files/documents/Burma_Narrative_TBRM21_TBDIAH_Version_Final.pdf

2. **Drug-Resistant Tuberculosis: A Survival Guide for Clinicians, 3rd edition** https://www.currytbcenter.ucsf.edu/products/view/drug-resistant-tuberculosis-survival-guide-clinicians-3rd-edition

3. **Guidance on requirements for QTc measurements in ECG monitoring when introducing new drugs** Guidance on requirements for QTc measurement in ECG monitoring when introducing new drugs and shorter regimens for the treatment of Multi/Extensively Drug-Resistant Tuberculosis (tbdiah.org)

4. **Linezolid an effective, safe, and cheap drug for patients failing multidrug-resistant tuberculosis treatment in India** https://erj.ersjournals.com/content/erj/39/4/956.full.pdf

5. **Nursing Guide for Managing Side Effects** https://www.currytbcenter.ucsf.edu/products/nursing-guide-managing-side-effects-drug-resistant-tb-treatment

6. **Patient-centered care, social support and adherence to treatment** https://apps.who.int/iris/bitstream/handle/10665/130918/9789241548809_eng.pdf?sequence=1&isAllowed=y

7. **Report of Expert Consultations on Rapid Molecular Testing to Detect Drug-Resistant Tuberculosis in the United States** https://www.cdc.gov/tb/topic/laboratory/rapidmoleculartesting/background.htm

8. **The effects of Bedaquiline and Fluoroquinolones based treatment regimens in patients with MDR/XDR TB on QT prolongation** The effects of bedaquiline and fluoroquinolone-based treatment regimens in patients with MDR/XDR-TB on QT prolongation | European Respiratory Society (ersjournals.com)

9. **The Spectrum of Tuberculosis from Infection to Disease, TB at a Glance, 3rd edition** https://www.heartlandntbc.org/assets/products/The_Spectrum_of_TB.pdf

10. **Treatment of Drug-Resistant Tuberculosis An Official ATS/CDC/ERS/IDSA Clinical Practice Guideline** https://www.cdc.gov/tb/publications/guidelines/pdf/Nahid_et_al-2019-American_Journal_of_Respiratory_and_Critical_Care_Medicine.pdf

QUESTIONS AND ANSWERS

1.) Does her previous TB treatment impact her current treatment plan?

a. Yes; she is from a high burden country and could have MDR-TB
b. No; she does not have documentation of treatment
c. Yes; she recalls taking medication "on and off for almost a year"
d. A & C

Rationale: History of previous treatment impacts her current treatment plan because the patient has two predictors of MDR-TB, which includes previous "on and off" TB treatment and is native of a country with high prevalence of MDR-TB.

2.) Based on the results from the MDDR report above, what can be concluded?

a. The patient has disseminated MDR-TB
b. There is an rpoB mutation that is consistent with rifampin resistance (RR)
c. The katG mutation is consistent with high level INH resistance
d. All of the above

Rationale: Multidrug-resistant TB (MDR-TB) is the definition of TB bacteria that is resistant to at least isoniazid and rifampin. rpoB gene mutation is associated with RR, and katG gene mutation is associated with INH resistance.

3.) Which condition or medication in her MDR-TB treatment might be attributing to symptoms that suggest development of a peripheral neuropathy (PN)?

a. It could be a side effect of linezolid
b. It could be a side effect of bedaquiline
c. It could be related to her diabetes
d. A & C

Rationale: PN is a side effect of linezolid when it is given for prolonged periods; however, diabetes can cause PN as well. Linezolid is one of the most effective drugs for treating MDR-TB. In this case, before stopping this drug, it's important to carefully evaluate the cause of PN.

4.) How do you interpret these results??

a. Abnormal value: Linezolid trough concentration level is too high
b. Abnormal value: Linezolid peak concentration level is too high
c. Both levels are in the normal range
d. Abnormal value: Peak level is too low

Rational: Both levels are in the normal range. Oral and intravenous linezolid doses of 600 mg every 12 hours produce a peak concentration in the range of 12-26 mcg/ml approximately 2 hours post oral doses. Trough linezolid concentration should be less than 2 mcg/ml. The results on this patient: peak concentration level: 15.9 mcg/ml; trough linezolid concentration: 1.2 mcg/ml.

5.) Which medication in her MDR-TB treatment regimen might have attributed to her palpitations and anxiety?

a. Linezolid
b. Moxifloxacin
c. Bedaquiline
d. B & C

Rationale: New DR-TB drugs, such as bedaquiline and delamanid, may prolong the QT interval in the electrocardiogram (ECG), as well as repurposed agents for DR-TB like moxifloxacin; if this symptom is not addressed in time, it may lead to life threatening arrhythmias, such as Torsade's de Pointes (TdP).

6.) Is the QTc result normal or abnormal for a female patient?

a. Normal
b. Abnormal

Rationale: The QTc is considered normal at <450 ms in males and <470 ms in females. It can vary by up to 75 ms in the same individual at different times during the same day. Because of this, it is recommended that the EKG for QTc monitoring be done at approximately the same time of the day. The QTcF is considered prolonged when it is ≥450 ms among males and ≥470 ms among females. It is considered dangerous when it is >500 ms for both males and females.

Monthly[1] Toxicity Monitoring by Medication Type

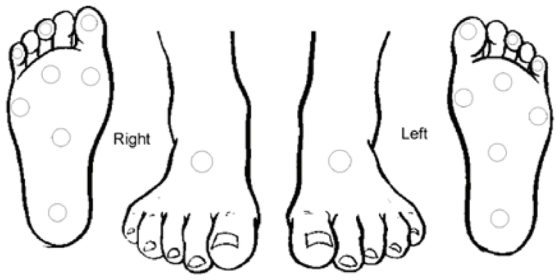
Medication	Assessment							
	Medical Assessment[2]	CBC/CMP	Ca++, K+, Mg++, and/or TSH	EKG	Mental Status Changes	Neuropathy Assessment	Visual Acuity/ Color Vision Assessment	Audiometry[3] /Vestibular Toxicity Assessment
Bedaquiline	Baseline, mo.	Baseline, mo.	Baseline, mo.	Baseline, mo. (preferred)[5]				
Moxifloxacin/ Levofloxacin	Baseline, mo.	Baseline, mo.		As indicated[6]				
Linezolid[4]	Baseline, mo.	Baseline, mo.				Baseline, mo.	Baseline, mo.	
Pretomanid	Baseline, mo.	Baseline, mo.	Baseline, mo.	Baseline, mo. (preferred)[5]				
Delamanid	Baseline, mo.	Baseline, mo.	Baseline, mo.	Baseline, mo. (preferred)[5]				
Clofazimine	Baseline, mo.	Baseline, mo.		As indicated[6]				
Cycloserine	Baseline, mo.	Baseline, mo.			Baseline, mo.			
Pyrazinamide	Baseline, mo.	Baseline, mo.						
Amikacin	Baseline, mo.	Baseline, mo.	Electrolytes only Baseline, mo.					Baseline, mo.
Streptomycin	Baseline, mo.	Baseline, mo.	Electrolytes only Baseline, mo.					Baseline, mo.
Ethionamide	Baseline, mo.	Baseline, mo.	TSH only Baseline, mo.			Baseline, mo.	Baseline, mo.	
Meropenem	Baseline, mo.	Baseline, mo.						

Ca++: Calcium; **K+:** Potassium; **Mg++:** Magnesium; **TSH:** thyroid stimulating hormone

1. Frequency of monitoring may be increased as indicated.
2. Medical assessment including weight, signs and symptoms of TB, indications of drug toxicity, drug-drug interactions; additional assessment as indicated including need for dose adjustment (based on renal function, weight, serum drug level, etc.).
3. 1000 Hz - 8000 Hz
4. Consider drug-drug interactions that might lead to serotonin syndrome.
5. Minimum requirement is baseline and at least weeks 2, 12, and 24.
6. Consider baseline EKG if other cardiac risk factors are present.

Peripheral Neuropathy Evaluation

Lower Extremities



PATIENT'S INTERVIEW (Ask your patient the following questions:

Question 1:

¿Do you have any pain in your feet?

Yes	No

Question 2: Does your pain have any of these characteristics?

		Yes	No
1	Burning?		
2	Freezing pain?		
3	Electric shock-type sensation?		

Question 3: Do you have any of these symptoms in the area?

		Yes	No
4	Tingling		
5	Prickling		
6	Numbness		
7	Stinging/itching		

Question 4: ¿ Is the pain made worse with the touch of clothing or bed sheets?

Yes	No

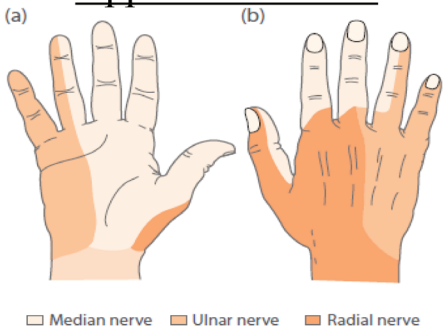
PATIENT'S ASSESSMENT

Question 5:

		Yes	No
8	Hypoesthesia to touch		
9	Hypoesthesia to prick		
10	Extreme sensitivity to touch		
11	Extreme sensitivity to prick		

Patient's name:
DOB:
Date of evaluation:

Upper Extremities



PATIENT'S INTERVIEW (Ask your patient the following questions:

Question 1:

¿ Do you have any pain in your hands?

Yes	No

Question 2: Does your pain have any of these characteristics?

		Yes	No
1	Burning		
2	Freezing pain?		
3	Electric shock-type sensation?		

Question 3: ¿Do you have any of these symptoms in the area?

		Yes	No
4	Tingling		
5	Prickling		
6	Numbness		
7	Stinging/Itching		

Question 5 Is the pain made worse with the touch of clothing or bed sheets?

Yes	No

PATIENT'S ASSESMENT

Question 4:

		Yes	No
8	Hypoesthesia to touch		
9	Hypoesthesia to prick		
10	Extreme sensitivity to touch		
11	Extreme sensitivity to prick		

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Notes:

Case Study 9

Cutaneous Drug Reaction

Cutaneous Drug Reaction

Objectives:

- Recognize the differences between a drug rash and a side effect.
- Identify and describe the characteristics of a typical drug rash.
- Prioritize nursing interventions when a drug rash occurs.
- Identify when a cutaneous reaction may warrant a drug re-challenge.

Case History:
A 26-year-old female, contact to a patient with pan-susceptible tuberculosis (TB) had a positive TB skin test (TST) during her second-round testing with accompanying productive cough, and 5 pound weight loss. The patient received a baseline work-up by the local health department which included a physical assessment, medical history, routine labs (CBC, CMP, HIV), induced sputum collection, and was educated on latent TB infection (LTBI) and active TB disease. The patient also received a referral for a chest x-ray (CXR) which resulted abnormal. After consulting with an expert Infectious disease (ID) physician, the Public Health Nurse (PHN) received recommendations to start the patient on the rifampin, isoniazid, pyrazinamide, and ethambutol (RIPE) by directly observed therapy (DOT) pending culture and susceptibilities.

Patient Education
Educating patients about their disease process and allowing them to ask questions will give them peace of mind which can aide in treatment adherence and overall good outcomes.

All baseline assessments came back within normal limits and the patient was given her first dose of RIPE in the clinic. She tolerated the medications well without any complications. After 5 days on RIPE, the patient developed a rash on her lower back and called the PHN to notify her.

1.) What questions should the nurse ask the patient? (Circle all that apply.)
a. Are you having difficulty breathing?
b. Have you recently started a new medication, soap/detergent, cologne, or moisturizer?
c. Is this rash spreading to other parts of your body?
d. When did you first notice the rash?
e. All of the above

2.) What is the most appropriate action for the nurse to take *first*? OR which of the following is the *most* important nursing intervention?
a. Document the patient's reaction in her chart.
b. Tell the patient to go to the closest emergency department.
c. Have the patient take some Benadryl and lay down.
d. Hold all TB medications.

The nurse proceeded to rule out the possibility of an anaphylactic reaction to the TB medications. She asked the patient if she was having difficulty breathing or swallowing and if the rash was spreading to other parts of her body. The PHN also asked if she had a fever or had any swelling to

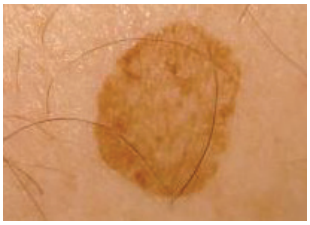
her eyes or lips; she denied these symptoms. The nurse continued to ask when she first noticed the rash, if she had allergies to any medications, and then asked her to go to the clinic for further questions and evaluation.

3.) Which of the following are common side effects of first line anti-tuberculosis medications?

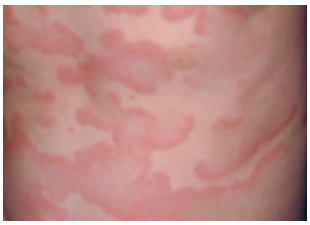
a. Orange body fluids
b. Swelling around the eyes or lips
c. Hives on the whole body
d. Fever

On arrival to the clinic the nurse asked the patient if she started using any new skin care products (e.g., lotion, body wash) or a new detergent that may be causing the rash. The patient stated she had not. The patient was asked to disrobe to allow the nurse to properly perform a skin assessment and determine if the rash was present in other parts of her body such as the neck, the abdomen, or other extremities. The PHN then inspected the location, texture, color, and size of her rash.

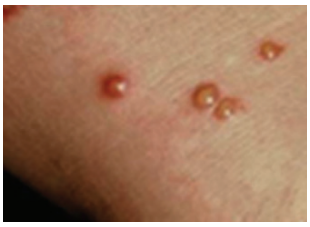
4.) Below are four pictures with cutaneous reactions. Please match each picture from the left-sided column to the appropriate description on the right-sided column.



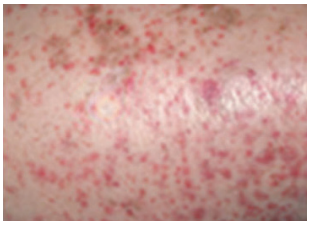
_____ **1** Hives (urticaria, wheals) are circumscribed, raised, erythematous plaques, often with central pallor. Lesions may be round, oval, or serpiginous (wavy margin) in shape and vary in size from less than 10mm to several centimeters in diameter. They are intensely itchy. Individual lesions are transient, usually appearing and enlarging over the course of minutes to hours and then disappearing within 24 hours. Lesions may coalesce (come together) as they enlarge.



_____ **2** Petechiae are non-blanchable and nonpalpable, pinpoint macules (less than a few millimeters in diameter) that result from capillary inflammation and red blood cell extravasation.



_____ **3** Macules are flat, nonpalpable, and of small diameter < 1 cm that vary in pigmentation from the surrounding skin. Examples of Macules include: rubella, measles, freckles, flat moles.



_____ **4** Papules are elevated lesions usually < 10 mm in diameter that can be felt or palpated. Examples include nevi, warts, insect bites, some lesions of acne.

https://www.merckmanuals.com/professional/dermatologic-disorders/approach-to-the-dermatologic-patient/description-of-skin-lesions

Cutaneous Drug Reaction

The nurse documented the patient's rash as mild macular lesions, non-raised, blanchable and erythematous, measuring between 5-7 mm in diameter and confined to the lower back. The patient expressed how she had plans to go play volleyball with her friends but was going to cancel because she was embarrassed of the way her back looked. The nurse very empathetically put her hand on the patient's shoulder and let her know that she was sorry this was happening to her. She explained that the symptoms were temporary and would subside.

> Nurses can help to strengthen relationships with their patients by showing sympathy when patients express their fears and concerns.

After the nurse completed her assessment, she re-consulted with the expert ID physician and asked for recommendations on how to proceed. The ID physician recommended to hold medications for 5 days and (once the rash was completely resolved) to begin a drug re-challenge to help identify the causative agent. They also recommended premedicating with a short-acting antihistamine 30 minutes before medication administration.

> All antituberculosis drugs have the possibility of causing cutaneous reactions. Management of adverse effects often requires consultation with a medical expert.

5.) **Why is it recommended to premedicate with a short-acting antihistamine?** (Please use the Heartland Drug Re-challenge Protocol for RIPE found on pages 88-89 to aid you in answering this question.)

a. To ensure the patient does not become nauseous.
b. In order to prevent or decrease a serious drug reaction.
c. To help overcome headaches associated with anti-tuberculosis drugs.
d. To enhance the efficacy of the anti-tuberculosis medications.

After 5 days off the TB medications, the patient's rash was resolved. The PHN explained to the patient the purpose of the drug re-challenge and let her know it would require her to come into the clinic each time a new drug was going to be introduced in order to premedicate and monitor her for side effects. The patient looked distraught and let the PHN know she had to be at school from 8 a.m. to 4 p.m. every day of the week. The nurse let the patient know that the clinic did not open until 8 a.m. but that she would open the clinic one hour earlier to accommodate her needs. Although the patient expressed it would be difficult for her to wake up even earlier, she was grateful for the nurses' efforts and agreed to show up at 7 a.m.

> It is important for nurses to work together with their patients and devise a plan that will ensure the patient's safety during treatment.

The following day the patient showed up to the clinic at 7 a.m., was premedicated with an antihistamine, and started the drug re-challenge with the re-introduction of rifampin.

6.) Which of the following best describes why it is important to start the re-challenge with rifampin? (Circle all that apply.)

a. Because it is the highest dose of medicine the patient will take.
b. Because it is the most important drug and will have the biggest impact on the treatment regimen if it can be used.
c. Because it metabolized faster.
d. If rifampin cannot be used, the patient will need to be treated as a drug resistant TB patient.

After 3 days of taking rifampin with no reaction, isoniazid was added to the regimen. On the fourth day, with the reintroduction of isoniazid, the patient developed a mild rash on her lower back despite being premedicated with an antihistamine. The rifampin and isoniazid were placed on hold until the rash completely resolved. It was determined that isoniazid was the culprit. As per the medical consultant ID expert recommendations, isoniazid was discontinued and replaced with a fluoroquinolone. The patient went on to complete 9 months of treatment without any further complications.

Additional Information:

- All drugs can cause allergic reactions that range from mild to severe or anaphylactic.
- Becoming familiar with other possible causes of rash may help discern if a cutaneous reaction is truly a drug reaction. Consider the following: scabies, heat rash, psoriasis, chigger bites, fungal infection, and bedbugs.
- If a patient experiences a drug-induced cutaneous reaction, it is important to document it in their medical chart and to include a detailed description of the reaction. Also, counsel the patient never to use the offending medication again.
- Taking a patient-centered approach by allowing the patient to ask questions and educating them about drug induced cutaneous reactions is important in maintaining a good relationship with your patient. This will reassure them that they can trust you with administering their medications for the remainder of the treatment.
- It is recommended to seek expert consultation from TB experts when there is the possibility of a drug-induced cutaneous reaction to TB medications. A TB expert can walk you through performing a drug re-challenge to RIPE and making the appropriate drug substitutions if necessary.

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Heartland Protocol for Drug Re-challenge with RIPE

EDIT THIS TEMPLATE PER SPECIFIC PATIENT – POSSIBLE TEXT TO BE EDITED PER PATIENT IN **RED**

Please hold anti-TB medications at least until rash is completely resolved. After the rash is resolved, a drug re-challenge can be initiated.

It is important to be cautious with a drug re-challenge. Start the re-challenge on a Monday or Tuesday, if possible, by introducing one new medication each week. It may take a few days for the rash to appear, and if you add a new drug every day or two, it may be unclear which is causing the problem. Pre-medicating the patient, as noted below, may not be needed, but it may prevent/decrease a serious drug reaction.

During the re-challenge always remember: **If any medication is not tolerated, stop it, identify/ document in the chart that the patient is allergic to the medication by the drug re-challenge, and describe the reaction. You must wait until the rash resolves for several days before trying the next medication.**

Re-challenge on Day 1 and 2 with each new medication should be done in the clinic if possible, and the patient should wait at least 30 minutes after the dose before he/she leaves. This will allow the HCW to assist the patient if a reaction does occur.

Start the re-challenge with rifampin first because it is the most important drug and will have the greatest impact on the treatment regimen if it can be used.

Re-challenge day # 1: Pre-medicate the patient a ½ hour prior to giving the first dose, with 25 mg of Benadryl and 20 mg of prednisone. Consider starting with rifampin 300mg. This should help to blunt a reaction if it occurs.

Re-challenge day # 2: If treatment is tolerated with rifampin 300 mg on day # 1, then on the second day, pre-medicate the patient as previously indicated with Benadryl 25 mg and prednisone 20 mg, and give rifampin 600 mg.

Re-challenge day # 3: If treatment is tolerated, then pre-medicate with Benadryl only and give 600 mg rifampin.

Re-challenge day # 4-6 (of 7): If day three rifampin 600 mg is tolerated by pre-medicating with Benadryl only, give rifampin 600 mg daily for several more days without any pre-medication. Continue rifampin through the weekend.

Make sure that the medication is taken over the weekend once a drug is successfully re-introduced. It is best to give the newly tolerated medication 7 days a week. Continue to ensure the patient does not miss a dose of rifampin if it is tolerated. If there is another interruption (and the re-challenge did help with tolerance), rash may recur.

The next drug to add is Isoniazid (INH). This should start the following week (week 2).
Re-challenge day #1, week 2: Pre-medicate the patient a ½ hour prior to the dose with 25 mg of Benadryl and 20 mg of prednisone. Give both rifampin 600mg and INH 150 mg.

Re-challenge day # 2, week 2: If rifampin and INH are tolerated, on day # 1, pre-medicate as previously indicated with Benadryl 25 mg and prednisone 20 mg then give 600 mg of rifampin and 300 mg of INH.

Re-challenge day #3, week 2: If day two medications are tolerated, on day three pre-medicate with 25 mg of Benadryl only and give rifampin 600 mg and INH 300 mg. If tolerated, continue rifampin and INH (no further pre-medication needed).

Day # 4-6 or 7, week 2: If day three rifampin 600 mg and INH 300 mg is tolerated with only Benadryl as a pre-medication, give rifampin 600 mg and INH 300 mg daily for several more days without any pre-medication. Continue both INH and rifampin through the weekend.

If you do not have susceptibility studies, you should also re-challenge with ethambutol. If you are able to successfully re-challenge with rifampin, INH and ethambutol, generally you would not re-challenge with PZA.

Continue the three drugs pending culture and susceptibility test results.

Re-challenge day #1, week 3: Pre-medicate the patient a ½ hour prior to the dose with 25 mg of Benadryl and 20 mg of prednisone. Give rifampin 600mg, INH 300 mg, and ethambutol 100mg.

Re-challenge day #2, week 3: If rifampin 600 mg, INH 300 mg, and ethambutol 100 mg is tolerated on day # 2, pre-medicate as previously indicated with Benadryl 25 mg and prednisone 20 mg, rifampin 600 mg, INH 300 mg, and give full dose of ethambutol.

Re-challenge day #3, week 3: If day two medications are tolerated, on day three pre-medicate with 25 mg of Benadryl only and give rifampin 600 mg, INH 300 mg and full dose ethambutol. If tolerated, continue rifampin INH, and ethambutol (no further pre-medication needed).

QUESTIONS AND ANSWERS

1.) What questions should the nurse ask the patient? (Circle all that apply.)

a. Are you having difficulty breathing?
b. Have you recently started a new medication, soap/detergent, cologne, or moisturizer?
c. Is this rash spreading to other parts of your body?
d. When did you first notice the rash?
e. All of the above.

Rationale: It is important to find the causative factor for the reaction. As the nurse, you must ask the appropriate questions to rule out if the reaction is a true anaphylactic reaction or a side effect to the medications. Finding out when the rash started and if it correlates with the start of RIPE may determine that RIPE is the causative agent.

2.) What is the most appropriate action for the nurse to take *first*? OR which of the following is the *most* important nursing intervention?

a. Document the patient's reaction in her chart.
b. Tell the patient to go to the closest emergency department.
c. Have the patient take some Benadryl and lay down.
d. Hold all TB medications.

Rationale: Although it is also important to document the reaction in the patient's chart, the most important thing to do first is to stop all TB medications. You do not want to ask a patient to take an antihistamine that may mask side effects until you have first assessed him/her. It is not necessary to ask the patient to go to the emergency department unless he/she is showing signs of an anaphylactic reaction.

3.) Which of the following are common side effects of first line anti-tuberculosis medications?

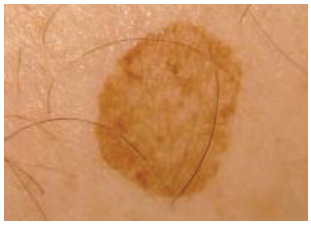
a. Orange body fluids
b. Swelling around the eyes or lips
c. Hives on the whole body
d. Fever

Rationale: Orange body fluids are a common side effect of rifamycins. Swelling around the eyes or lips, hives, and fever all indicate a life-threatening allergic reaction.

Cutaneous Drug Reaction

4.) Below are four pictures with cutaneous reactions. Please match each picture from the left-sided column to the appropriate description on the right-sided column.

3



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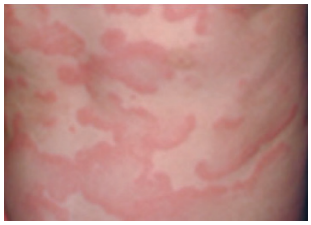
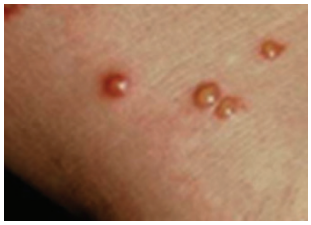
1



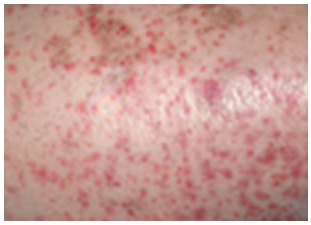
Petechiae are non-blanchable and nonpalpable, pinpoint macules (less than a few millimeters in diameter) that result from capillary inflammation and red blood cell extravasation.

4



Macules are flat, nonpalpable, and of small diameter < 1 cm that vary in pigmentation from the surrounding skin. Examples of Macules include: rubella, measles, freckles, flat moles.

2



Papules are elevated lesions usually < 10 mm in diameter that can be felt or palpated. Examples include nevi, warts, insect bites, some lesions of acne.

https://www.merckmanuals.com/professional/dermatologic-disorders/approach-to-the-dermatologic-patient/description-of-skin-lesions

Rationale: Typical drug rashes are systemic, starting in any part of the body and spreading to other areas, and lasting 2 to 21 days. A typical drug rash will manifest as macular, popular, pruritic, or erythematous.

5.) Why is it recommended to premedicate with a short acting antihistamine? (Please us the Heartland Drug Re-challenge Protocol for RIPE found on pages 88-89 to aid you in answering this question.)

a. To ensure the patient does not become nauseous.
b. In order to prevent or decrease a serious drug reaction.
c. To help overcome headaches associated with anti-tuberculosis drugs.
d. To enhance the efficacy of the anti-tuberculosis medications.

Rationale: Premedicating may aide in preventing/decreasing a serious drug reaction. Many times if the patient has a reaction to an anti-tuberculosis medication the antihistamine will blunt the effect, so it will not cause serious harm to the patient.

6.) Which of the following best describes why it is important to start the drug re-challenge with rifampin? (Circle all that apply.)

a. Because it is the highest dose of medicine the patient will take.

b. Because it is the most important drug and will have the biggest impact on the treatment regimen if it can be used.

c. Because it metabolized faster.

d. If rifampin cannot be used, the patient will need to be treated as a drug resistant TB patient.

Rationale: Rifampin is fundamental for the treatment of tuberculosis. If a patient is not able to have rifampin in their treatment regimen, they will require a longer and often more intense treatment. Rifampin should be challenged, when possible, to ensure the patient is given the most adequate treatment.

Notes:

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Consultation to healthcare providers at 1-800-TEX-LUNG
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