

Take a Deep Breath: A Case of Respiratory Illness

by

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Part I – Symptoms

Callie was 26 years old when she opened a bakery called “Callie’s Cupcakes” in downtown San Francisco with her fiancé, Jeremy. Despite the competitive market, her business was booming; everyone loved the clever recipes and the trendy atmosphere. Between running their fast-growing business and planning for their wedding, Callie hadn’t been able to keep to her usual eight hours of sleep a night. Although she had always lived a very healthy lifestyle, exercising daily and eating healthy, she just hadn’t been feeling herself lately. She was tired all the time, had difficulty breathing, felt stressed, coughed up sputum, consistently ran a low-grade fever, and had lost weight as her appetite decreased. None of these symptoms alone had been particularly alarming so she had put off seeing her physician for a few weeks.

Questions

1. What are Callie’s symptoms? List all that were mentioned.
2. Based on the symptoms presented, what are *three* possible respiratory infectious diseases Callie could be suffering from? Explain why.
3. Based on Callie’s symptoms and your answers so far, it seems Callie is having trouble with her respiratory system. Several respiratory conditions can impact gas exchange. Describe the process of gas exchange in the lung (alveoli).

Part II – The Diagnosis

As each day passed Callie's symptoms grew worse and worse. After standing for long periods of time she could barely breathe; in fact, she couldn't even work a full day in the bakery without feeling like she was going to pass out. When it got to the point that extreme exhaustion and high fever prevented her from getting out of bed, Jeremy was alarmed. "Callie, I'm taking you to see your doctor," he said, and got her an appointment for the next morning.

Once there, Callie explained to her physician, Dr. Nayak, that she had been tired, fatigued, stressed, and that she hadn't been sleeping well. She also mentioned that she had lost some weight and just didn't have an appetite. The worst part was the shortness of breath and the cough. Her breathing troubles and coughing had lasted for about three weeks and seemed to be getting worse. As a precaution, Dr. Nayak decided to provide Callie a surgical mask in case she had an infectious respiratory disease. She then proceeded to do a basic physical exam as well as a chest x-ray and a sputum analysis.

Dr. Nayak then asked Callie if she had traveled out of the country within the past three months. Callie looked confused, and said "no." The doctor followed this up by asking whether Callie had come into contact with anyone who had been out of the country. Thinking about it for a moment she replied, "Well, one of the employees in our bakery is from South Africa and she frequently visits her family back at home; she's actually in South Africa visiting right now. I work with her weekly. Could that really be a factor?"

"Yes, it could," Dr. Nayak said. "Did your employee have any symptoms that you can recall?"

Callie reflected a moment and said, "Yes, she does seem to always have a cough. She told me it was just allergies and that she might be bothered by all the flour in the air."

The chest x-ray came back and showed nodular formations in both of Callie's lungs near the clavicles. Based on the x-ray and symptoms, Dr. Nayak suspected Callie had tuberculosis, more specifically active tuberculosis, also known as tuberculosis disease. South Africa has one of the highest incidences of active TB in the world, and knowing that Callie had an employee who frequently visited that location made Dr. Nayak suspect TB, but they would need to run some tests to be sure. Dr. Nayak's local laboratory lacked the most rapid testing mechanisms, so it would take a few days to receive results from the sputum stain and the sputum nucleic amplification test. Dr. Nayak also took a blood sample for additional testing. Due to her suspicion for TB, Dr. Nayak advised Callie to stay home and not work until they could confirm her diagnosis. She provided Callie with some surgical masks in the event she needed to go out. After Callie left, Dr. Nayak contacted the local health department and reported that she suspected her patient had TB.

Questions

4. What is the causative agent for tuberculosis (TB)? How does one get tuberculosis?

5. Explain the tests used to diagnose someone with active TB (make sure to include x-ray, sputum analysis, skin tests, and blood tests). Use the following website for help: <http://www.merckmanuals.com/home/infections/tuberculosis-and-leprosy/tuberculosis-tb>.

6. Using information from the Centers for Disease Control and Prevention (CDC) and the link in the previous question, compare and contrast latent TB with active TB (also called TB disease). Fill out the table below, then add in the information we know so far about Callie. See: <https://www.cdc.gov/tb/publications/factsheets/general/ltbiandactivetb.pdf>.

	Latent TB	Active TB (TB Disease)	Callie
Causative agent			
Signs/symptoms			
X-ray results			
Sputum stain			
Sputum culture			
Skin test			
Blood test			
Contagious (yes/no)			

7. Based on the data available so far, can you tell if Callie has an active or latent TB infection? Explain your reasoning.

Part III – Impacts on Lung Function

After a few days had passed, Callie and Jeremy returned to Dr. Nayak's office and were told that Callie's sputum stain was positive, as was her blood test. The nucleic amplification test results showed that Callie did in fact have active TB. Dr. Nayak informed Callie that she needed to contact her employee right away for testing; all other employees of the bakery also needed to be tested, including Jeremy. Callie replied that a nurse from the health department had already visited with her and had begun the contact investigation.

Jeremy was concerned for Callie and asked for more details. Dr. Nayak explained that active TB is caused by the presence of active bacteria, *M. tuberculosis*, in the body. The bacteria initially enter the body via the respiratory system, and in active infection they can be found in the lung as well as in other body tissues. When the bacteria initially enter the alveoli the body's immune cells, macrophages, attack the bacteria. If the macrophages are successful, the bacteria are removed and the infection ends. If they cannot completely kill the bacteria those bacteria begin to replicate inside the macrophage. The macrophage then dies thus triggering an additional immune response and inflammation (increased blood flow and fluid/pus production). This inflammation can result in difficulty breathing and cell granulomas (nodular areas that contain the bacteria and immune cells), which can further impact respiratory function in the alveoli. Dr. Nayak provided Jeremy and Callie with the following link to a YouTube video so that they could learn more about the disease at home: <https://youtu.be/0qFifLL21U>.

Dr. Nayak then told Callie that she was actually lucky; Dr. Nayak had also ordered a test to check the sputum sample for drug susceptibility. The results showed that Callie had a type of TB that would respond to first-line antibiotics; in other words, she was not infected with a drug-resistant strain.

Jeremy nodded along as Dr. Nayak spoke, but when the physician left the room, he turned to Callie and admitted he was still confused about how this impacted breathing. Callie thought for a minute and then recalled what she had learned when she took introduction to physiology in college. She explained that the alveoli, the little grape-like sacs in the lungs, are used for gas exchange. The alveoli have thin walls, a large surface area, and make contact with vast capillary beds—they are prime locations for swapping of gases.

While Callie was talking, Jeremy pulled out his smartphone and found the following:

*Fick's law can be used to determine the diffusion rate across a surface. The equation states: diffusion rate = (area * concentration gradient of gas [partial pressure in lung vs. blood] * surface permeability [diffusion constant or coefficient]) / membrane thickness². Thus, diffusion is fastest if the concentration gradient is high, the membrane is thin (and permeable), and exchange surface is large.*

Questions

8. Based on what you know and what you have just read, how do you think active TB infection impacts gas exchange in the alveoli? (*Hint: think about which aspect of Fick's law is being altered.*)

9. Based on what you know about Callie, are there any life style factors that might be contributing to her health and respiratory problems? Specifically, could something have exacerbated her condition? Explain.

Part IV – TB Contraction and Treatment

Dr. Nayak's office coordinated with the nurse at the health department to begin Callie's treatment. Callie was prescribed four different antibiotics to kill off the *M. tuberculosis* bacteria. TB can be serious and prone to drug resistance so disease is always treated with multiple antibiotics. Callie was instructed to take her antibiotics, isoniazid, rifampin, pyrazinamide and ethambutol, with oversight of the public health nurse. Her total treatment might last 6–9 months. The health department nurse would provide Callie's medications at no charge and case manage her treatment to assure that Callie did not become drug resistant or suffer from side effects (e.g., hepatotoxicity, interference with oral birth control). Callie would also need to take off work and limit her contact with others as active TB is moderately contagious. Callie would likely be non-contagious after two to three weeks of treatment and could return to her bakery at that time.

After returning home from her doctor's appointment, Callie decided to search for information on the internet about TB. Although she had learned something about the pathophysiology of TB and had received a prescription from her physician, she still wanted to know more about how she could have become infected. She was also interested in how tests for TB work. She wanted to know more, but there were just so many websites with conflicting information; she needed help sorting it all out.

Answer the following questions, using the CDC or WHO, to help Callie find the reliable information she needs.

Questions

10. Based on the information that Callie gave her doctor, how could she have contracted tuberculosis? How is pulmonary tuberculosis transmitted?

11. Can a person with latent TB pass it to others?

12. When looking up information Callie discovered that people can have false positive results to the tuberculin skin test. Describe the tuberculosis skin test (TST) and explain why a false positive can occur.

13. Jeremy and all of Callie's coworkers were identified as close contacts by the health department nurse. They all underwent tuberculosis skin testing. If Jeremy and Callie's coworkers have positive TSTs, would you interpret them as false positives or an indication of latent TB infection?



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