Tuberculosis

FACT SHEET

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Summary

Tuberculosis (TB) is caused by bacteria called *Mycobacterium tuberculosis* complex and usually affects the lungs. However, among people co-infected with TB and HIV, parts of the body outside the lungs are often affected; this is called extra-pulmonary TB.

The germs that cause TB are spread when a person inhales tiny droplets produced by people who have infectious, or active, TB of the lungs. TB infection can result in two different states—latent infection (which is symptom free) or active infection.

If left untreated, TB can be fatal and can be spread to other people. However, timely treatment, consisting of combination therapy with antibiotics, can cure both latent and active TB. Having had TB in the past—either the latent or active form of the disease—does not protect a person from future infection with TB-causing bacteria.

What is TB?

Tuberculosis (TB) is an infection caused by bacteria called *Mycobacterium tuberculosis* complex. It usually affects the lungs, but in people co-infected with TB and HIV, parts of the body outside the lungs are often affected; this is called extra-pulmonary TB.

TB-causing bacteria are most commonly transmitted when someone inhales tiny droplets released into the air by an infected person during the following activities:

- coughing
- sneezing
- speaking

These tiny droplets are invisible and can remain floating in the air for several hours after they have been released.

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Transmission of TB-causing bacteria from an infectious person depends on many factors, including the following:

- how close or for how long a person was exposed
- the degree of infectiousness of the person with TB
- the type of shared environment in which contact took place

Studies have found that people with TB whose sputum (the thick mixture that people with chest infections produce when they cough) contains TB-causing bacteria are likely to transmit these bacteria. Also, people with cavities in their lungs caused by TB are very infectious.

In high-income countries such as Canada, HIV-positive people exposed to TB-causing germs are prone to have TB-causing bacteria affect other parts of the body, including the following:

- the membranes surrounding the brain
- lymph nodes
- spleen
- liver
- kidneys
- bones

Infection with TB-causing germs can result in one of two forms of infection:

- latent TB infection – a person does not have symptoms and is not infectious
- active TB infection – a person has symptoms of illness and can spread TB-causing bacteria

Who is at risk for TB?

The risk of a person developing active disease from TB-causing bacteria after exposure depends on many factors, including the following:

- their overall health
- age – older people tend to have weaker immune systems
- among HIV-positive people, the lower the CD4 count, the greater the risk of developing TB

In general, after exposure to TB-causing bacteria, disease does not immediately result. Instead what usually happens once the bacteria enter the lungs is that they are captured by cells of the immune system. Sometimes the immune system is able to destroy these bacteria. At other times the bacteria are able to subvert the immune system's defences and go on to infect cells of the immune system. Once this happens, the infection can begin to spread slowly. For most people, at least initially, their immune system, if it does not kill the bacteria, is able to put the infection into a latent state. However, people whose immune systems are weakened by the following factors are at risk for ultimately developing active TB:

- HIV infection
- alcoholism
- diabetes
- injecting street drugs
- use of transplant drugs
- smoking tobacco

Symptoms

People with latent TB do not have symptoms; tests are needed to help assess their condition.

The symptoms of active TB can vary depending on the person and the organ-system affected. However, the following symptoms tend to be relatively common:

- unexpected tiredness
- fever
- night sweats
- unintentional weight loss
- swollen lymph nodes

In cases where TB has affected the central nervous system (CNS)—the brain and spinal cord—additional symptoms might include the following:

- severe headache

- confusion
- extremely stiff neck

In cases where TB-causing bacteria have spread throughout the body, the following symptoms may be present:

- night sweats
- loss of appetite
- weakness

In cases where TB has affected the lungs, the following symptoms can occur:

- persistent coughing
- coughing up blood
- chest pain

When examining a person with active TB, doctors may find that the following parts of the body are swollen:

- liver
- spleen
- lymph nodes

Diagnosis

Latent TB

To help diagnose latent TB, nurses can inject purified protein from TB-causing bacteria just under the skin (this does not cause infection). People with latent TB are very likely to have a reaction—usually a swelling or bump at the injection site within 48 to 72 hours.

The test is imperfect, and in people with severely weakened immune systems there may not be a reaction. In other cases, people infected with bacteria closely related to those that cause TB might develop a reaction. In some clinics, a blood test may also be used to help identify people with latent TB. These tests check for the presence of a chemical signal—interferon gamma—produced by the immune system.

Active TB

Doctors rely on several aids to help them diagnose active TB, including the following:

- X-rays
- examining fluid taken from an affected lymph node or organ under a microscope
- attempting to grow TB bacteria in the lab from fluid samples taken from a swollen lymph node or affected organ

Treatment

Latent TB

Usually a long course (between six and nine months) of the antibiotic isoniazid is prescribed. Treatment is prolonged because antibiotics work when the TB-causing bacteria are dividing, and in the case of latent TB, these bacteria grow very slowly.

Active TB

Due to widespread use of antibiotics and other factors, including improper adherence to therapy, TB-causing bacteria have developed varying degrees of resistance to therapy. In high-income countries like Canada, the U.S., Australia and Western Europe, once the diagnosis of active TB is made, it is often standard procedure to have a fluid sample (from the lungs or other affected tissue) taken and the TB bacteria tested in the lab for their ability to resist antibiotics.

Treatment of TB has two goals:

- to improve the health of people with TB by curing them of this infection
- to make patients non-infectious

The most common first-line treatment of active TB is a combination of the following antibiotics:

- isoniazid
- rifampin
- pyrazinamide
- ethambutol

Additional first-line agents include the following:

- rifabutin (Mycobutin) – sometimes prescribed in place of rifampin for HIV-positive people
- streptomycin – not commonly used in high-income countries

In HIV-positive people, doctors initiate potent combination therapy for HIV (commonly called ART) as soon as possible once TB has been diagnosed, as this helps improve the chances of recovery and survival. Doctors may also have to adjust antibiotic regimens or ART to reduce potential drug interactions.

HIV-positive people co-infected with TB are at risk for developing IRIS—immune reconstitution inflammatory syndrome. This occurs because when ART is initiated, the immune system is strengthened and begins to recognize and fight germs that it previously was unable to recognize and fight. As a result, symptoms of an infection (such as TB) may temporarily appear or may temporarily grow worse. Symptoms of IRIS can appear anywhere from two weeks to two years after ART has been initiated and are inflammation related. These can include fever, swollen lymph nodes and other symptoms depending on the type of infection and organ affected.

In some cases, such as in TB-related IRIS, drugs such as corticosteroids may be prescribed to help reduce symptoms caused by inflammation. IRIS tends to occur in people who have very low CD4 counts (less than 50 cells).

Additional antibiotics for the treatment of TB are available, but these, particularly second-line agents, tend to have more side effects, may have to be injected and may require extended courses of therapy. This is the case when treating multi-drug resistant (MDR)-TB.

New antibiotics for the treatment of TB are being tested.

Drug resistance

Shortly after the introduction of antibiotics in the 1950s, TB-causing bacteria began to develop resistance to one or more agents. Resistance to therapy is an important issue in TB treatment for the following reasons:

- Antibiotics generally used for TB are several decades older than newer antibiotics routinely used for the treatment of other bacterial diseases. Not surprisingly, TB drugs have unpleasant side effects—factors that do not encourage regular pill taking.
- After a few weeks or months of TB treatment, people begin to feel better and may arrive at the mistaken conclusion that they are cured. Consequently, they might prematurely stop taking antibiotics.
- In some conditions, such as HIV co-infection, TB antibiotics may not be well absorbed.

Infection with drug-resistant TB bacteria can have serious consequences for affected people. Not only do regimens become more complex and expensive, but also the risk of death increases. For instance, researchers from Quebec have found that resistance to the antibiotic pyrazinamide is associated with an increased risk of death. Researchers with the U.S. Centers for Disease Control and Prevention (CDC) have found that people who have TB that is resistant to rifampin or rifabutin are also at increased risk of death.

Second-line therapy

In Canada, agents for second-line therapy are available in cases of drug-resistant TB. However, drugs used in second-line therapy generally have more side effects, may need to be injected and are less effective than first-line agents. Examples of drugs used for second-line therapy include the following:

- moxifloxacin, levofloxacin
- amikacin, capreomycin, kanamycin
- ethionamide
- cycloserine
- para-aminosalicylic acid
- thiacetazone

Third-line agents

Strains of TB-causing bacteria that are resistant to two or more antibiotics are called multiple drug resistant (MDR-TB). Risk factors for developing resistance to second-line therapy include being HIV positive, having MDR-TB and having initial TB therapy with any second-line agent. In such cases of resistance, third-line agents are used, which can include antibiotics such as linezolid (Zyvox, Zyvoxam), clofazimine and clarithromycin. They have not generally been tested in large clinical trials for the treatment of TB. Several drugs are being developed for the treatment of TB.

Strains of TB-causing bacteria that are resistant to at least isoniazid and rifampin, and at least moxifloxacin or levofloxacin and at least one second-line injectable antibiotic are called extremely drug-resistant (XDR-TB). Such strains of TB are very hard to treat and require prolonged courses of antibiotics.

Prevention

The Bacille Calmette-Guérin (BCG) vaccine partially protects against TB infection. In Canada, this vaccine is not widely used and is only provided to infants of First Nations and Inuit communities with high rates of TB.

ART reduces the risk of illness due to AIDS-related infections, but research suggests that HIV-positive people continue to have an elevated risk for developing TB compared to healthy HIV-negative people.

Starting ART before the immune system is severely weakened and getting tested for latent infection with TB are important steps to reduce the risk of developing disease caused by TB.

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