Specific Infections

TUBERCULOSIS (TB)

Is an infectious disease usually caused by ***Mycobacterium tuberculosis (MTB) bacteria***. Tuberculosis generally affects the *lungs*, but can also affect other parts of the body.

Most infections show no symptoms, in which case it is known as ***latent tuberculosis***. About 10% of latent infections progress to active disease which, if left untreated, kills about half of those affected.

Typical symptoms of active TB are a chronic cough with blood-containing mucus, fever, night sweats, and weight loss. It was historically called consumption due to the weight loss. Infection of other organs can cause a wide range of symptoms.

Tuberculosis is spread from one person to the next through the air when people who have active TB in their lungs cough, spit, speak, or sneeze.

People with latent TB do not spread the disease. Active infection occurs more often in people with HIV/AIDS and in those who smoke. Diagnosis of active TB is based on chest X-rays, as well as microscopic examination and culture of body fluids.

Diagnosis of Latent TB relies on the tuberculin skin test (TST) or blood tests.

Active TB:

Pulmonary:

If a tuberculosis infection does become *active,* it most commonly involves the lungs (in about 90% of cases). Symptoms may include:

1. Chest pain.

2. Prolonged productive cough.

3. About 25% of people may not have any symptoms (i.e. they remain *asymptomatic*).

4. Occasionally, people may cough up blood in small amounts (hemoptysis), and in very rare cases, the infection may erode into the pulmonary artery or a Rasmussen's aneurysm, resulting in *massive bleeding*.

Tuberculosis may become a *chronic illness* and cause extensive scarring in the upper lobes of the lungs. The *upper lung lobes* are more frequently affected by tuberculosis than the lower ones. The reason for

this difference is not clear. It may be due to either better air flow, or poor lymph drainage within the upper lungs.

Extrapulmonary:

In 15–20% of active cases, the infection spreads outside the lungs, causing other kinds of TB. These are collectively denoted as ***extrapulmonary tuberculosis.***

Extrapulmonary TB occurs more commonly in people with a weakened immune system and young children. In those with HIV, this occurs in more than 50% of cases. Notable extrapulmonary infection sites include:

1. The pleura (in tuberculous pleurisy).
2. The central nervous system (in tuberculous meningitis).
3. The lymphatic system.
4. The genitourinary system (in urogenital tuberculosis).
5. The bones and joints.
6. A potentially more serious, widespread form of TB is called "disseminated tuberculosis", it is also known as miliary tuberculosis.

Causes:

The main cause of TB is ***Mycobacterium tuberculosis (MTB)***, a small, aerobic, nonmotile bacillus. In nature, the bacterium can grow only within the cells of a host organism, but M. tuberculosis can be cultured in the laboratory.

Using histological stains on expectorated samples from sputum, scientists can identify MTB under a microscope. Since MTB retains certain stains even after being treated with acidic solution, it is classified as an acid-fast bacillus. The most common acid-fast staining techniques are the Ziehl–Neelsen stain.

Transmission:

When people with active pulmonary TB cough, sneeze, speak, sing, or spit, they expel infectious aerosol droplets. Each one of these droplets may transmit the disease, since the infectious dose of tuberculosis is very small (the inhalation of fewer than 10 bacteria may cause an infection).

People with prolonged, frequent, or close contact with people with TB are at particularly high risk of becoming infected, with an estimated 22% infection rate. A person with active but untreated tuberculosis may infect 10–15 (or more) other people per year. Transmission should occur from only people with active TB – those with latent infection are not thought to be contagious.

The probability of transmission from one person to another depends upon several factors:

1. The number of infectious droplets expelled by the carrier.
2. The effectiveness of ventilation.
3. The duration of exposure.
4. The virulence of the M. tuberculosis strain.
5. The level of immunity in the uninfected person.

Risk factors:

A number of factors make individuals more susceptible to TB infection and/or disease.

Active disease risk:

I. The most important risk factor globally for developing active TB is concurrent HIV infection; 13% of those with TB are also infected with HIV.

II. Use of certain medications, such as corticosteroids.

III. Alcoholism.

IV. Diabetes mellitus (3-fold increased risk).

V. Silicosis (30-fold increased risk).

VI. Tobacco smoking (2-fold increased risk).

VII. Indoor air pollution and malnutrition.

VIII. Young age.

Pathogenesis:

About 90% of those infected with M. tuberculosis have asymptomatic, latent TB infections (sometimes called LTBI), with only a 10% lifetime chance that the latent infection will progress to overt, active tuberculous disease. In those with HIV, the risk of developing active TB increases to nearly 10% a year. If effective treatment is not given, the death rate for active TB cases is up to 66%.

The primary site of infection in the lungs, known as the **Ghon focus**, is generally located in either the upper part of the lower lobe, or the lower part of the upper lobe. Tuberculosis of the lungs may also occur via infection from the blood stream. This is known as a **Simon focus** and is typically found in the top of the lung. This hematogenous transmission can also spread infection to more distant sites, such as peripheral lymph nodes, the kidneys, the brain, and the bones. All parts of the body can be

affected by the disease, though for unknown reasons it rarely affects the heart, skeletal muscles, pancreas, or thyroid.

If TB bacteria gain entry to the blood stream from an area of damaged tissue, they can spread throughout the body and set up many foci of infection, all appearing as tiny, white tubercles in the tissues. This severe form of TB disease, most common in young children and those with HIV, is called **miliary tuberculosis**, people with this disseminated TB have a high fatality rate even with treatment (about 30%).

Diagnosis:

Active tuberculosis:

Diagnosing active tuberculosis based only on signs and symptoms is difficult, as is diagnosing the disease in those who have a weakened immune system.

A diagnosis of TB should, however, be considered in those with signs of lung disease.

1. Constitutional symptoms lasting longer than two weeks.

2. A chest X-ray.

3. Multiple sputum cultures for acid-fast bacilli are typically part of the initial evaluation.

A definitive diagnosis of TB is made by identifying M. tuberculosis in a clinical sample (e.g., sputum, pus, or a tissue biopsy). However, the difficult culture process for this slow-growing organism can take two to six weeks for blood or sputum culture. Thus, *treatment is often begun before cultures are confirmed.*

Latent tuberculosis:



Mantoux tuberculin skin test:

The Mantoux tuberculin skin test is often used to screen people at high risk for TB. Those who have been previously immunized with the BCG vaccine may have a *false-positive test result*. The test may be falsely

negative in those with sarcoidosis, Hodgkin's, lymphoma, malnutrition, and most notably, active tuberculosis.

Prevention:

Tuberculosis prevention and control efforts rely primarily on the vaccination of infants and the detection and appropriate treatment of active cases.

Vaccines:

The only available vaccine is Bacillus Calmette-Guérin (BCG). In children it decreases the risk of getting the infection by 20% and the risk of infection turning into active disease by nearly 60%.

It is the most widely used vaccine worldwide, with more than 90% of all children being vaccinated. The immunity it induces decreases after about ten years. As tuberculosis is uncommon in most of Canada, Western Europe, and the United States, BCG is administered to only those people at high risk. Part of the reasoning against the use of the vaccine is that it makes the tuberculin skin test falsely positive, reducing the test's usefulness as a screening tool. Several vaccines are being developed.

Treatment:

Treatment of TB uses antibiotics to kill the bacteria. Effective TB treatment is difficult, due to the unusual structure and chemical composition of the mycobacterial cell wall, which hinders the entry of drugs and makes many antibiotics ineffective.

Active TB:

Is best treated with combinations of several antibiotics to reduce the risk of the bacteria developing antibiotic resistance.

Latent TB:

Latent TB is treated with either isoniazid or rifampin alone, or a combination of isoniazid with either rifampicin or rifapentine.

The treatment takes three to nine months depending on the medications used. People with latent infections are treated to prevent them from progressing to active TB disease later in life.

New onset:

The recommended treatment of new-onset pulmonary tuberculosis is *six months of a combination of antibiotics containing* ***rifampicin, isoniazid, pyrazinamide, and ethambutol*** *for the first two months, and only* ***rifampicin and isoniazid*** *for the last four months*, where resistance

to isoniazid is high, ethambutol may be added for the last four months as an alternative.

Treatment with anti-TB drugs for at least 6 months results in higher success rates when compared with treatment less than 6 months; even though the difference is small. Shorter treatment regimen may be recommended for those with compliance issues.

Recurrent disease:

If tuberculosis recurs, testing to determine which antibiotics it is sensitive to is important before determining treatment. If multiple drug-resistant TB (MDR-TB) is detected, treatment with at *least four effective antibiotics for 18 to 24 months is recommended.*

TETANUS

Tetanus, also known as lockjaw, is a bacterial infection characterized by muscle spasms. In the most common type, the spasms begin in the jaw and then progress to the rest of the body.

Each spasm usually lasts a few minutes. Spasms occur frequently for three to four weeks. Some spasms may be severe enough to fracture bones.

Other symptoms of tetanus may include, fever, sweating, headache, trouble swallowing, high blood pressure, and a fast heart rate. Onset of symptoms is typically three to twenty-one days following infection.

Tetanus is caused by an infection with the **bacterium Clostridium tetani**, which is commonly found in soil, dust, the bacteria generally enter through a break in the skin such as a cut or puncture wound by a contaminated object, they produce toxins that interfere with normal muscle contractions.

Diagnosis is based on the presenting signs and symptoms, the disease does not spread between people.

The wound should be cleaned and any dead tissue should be removed, in those who are infected, tetanus immune globulin or, if unavailable, intravenous immunoglobulin (IVIG) is used.

Muscle relaxants may be used to control spasms, mechanical ventilation may be required if a person's breathing is affected.

Tetanus occurs in all parts of the world but is most frequent in hot and wet climates where the soil has a high organic content. Sign and **Symptom:**

Tetanus often begins with mild spasms in the jaw muscles—also known as lockjaw or trismus. The spasms can also affect the facial muscles

resulting in an appearance called risus sardonicus. Chest, neck, back, abdominal muscles and buttocks may be affected. Back muscle spasms often cause arching, called opisthotonos.

Sometimes the spasms affect muscles of breathing, which can lead to breathing problems.

Prolonged muscular action causes sudden, powerful, and painful contractions of muscle groups, which is called "***tetany***". These episodes can cause fractures and muscle tears.

Other symptoms include fever, headache, restlessness, irritability, feeding difficulties, breathing problems, burning sensation during urination, urinary retention and loss of stool control.

Even with treatment, about 10% of people who contract tetanus die. The mortality rate is higher in unvaccinated people and people over 60 years of age.

Incubation period:

The incubation period of tetanus may be up to several months, but is usually about ten days. *In general, the farther the injury site is from the central nervous system, the longer the incubation period*. The shorter the incubation period, the more severe the symptoms.

Generalized tetanus:

Generalized tetanus is the most common type of tetanus, representing about 80% of cases. The generalized form usually presents with a ***descending pattern***. The first sign is trismus or lockjaw, and the facial spasms are called risus sardonicus, followed by stiffness of the neck, difficulty in swallowing, and rigidity of pectoral and calf muscles. Other symptoms include elevated temperature, sweating, elevated blood pressure, and episodic rapid heart rate. Spasms may occur frequently and last for several minutes with the body shaped into a characteristic form called *opisthotonos*. Spasms continue for up to four weeks, and complete recovery may take months.

Causes:

Tetanus is caused by the tetanus bacterium Clostridium tetani. Tetanus is an international health problem, as C. tetani endospores are ubiquitous. Endospores can be introduced into the body through a puncture wound (penetrating trauma). Due to C. tetani being an anaerobic bacterium, it and its endospores thrive in environments that lack oxygen, such as a puncture wound. With the changes in oxygen levels, the drum stick-shaped endospore can result in quick spread.

Diagnosis:

There are currently ***no blood tests*** for diagnosing tetanus. The diagnosis is based on the ***presentation*** of tetanus symptoms and does not depend upon isolation of the bacterium, which is recovered from the wound in only 30% of cases and can be isolated from people without tetanus.

The "***spatula test***" is a clinical test for tetanus that involves touching the posterior pharyngeal wall with a soft-tipped instrument and observing the effect. A positive test result is the involuntary contraction of the jaw (biting down on the "spatula") and a negative test result would normally be a gag reflex attempting to expel the foreign object.

Prevention:

Unlike many infectious diseases, recovery from naturally acquired tetanus does not usually result in immunity to tetanus, this is due to the extreme potency of the tetanospasmin toxin. Tetanospasmin will likely be lethal before it will provoke an immune response.

Tetanus can be prevented by ***vaccination*** with tetanus toxoid, the CDC (centers for disaeses control) recommends that adults receive a booster vaccine every ten years, and standard care practice in many places is to give the booster to any person with a puncture wound who is uncertain of when he or she was last vaccinated, or if he or she has had fewer than three lifetime doses of the vaccine.

Treatment:

Mild tetanus:

Mild cases of tetanus can be treated with:

1. ***Tetanus immunoglobulin (TIG)***, also called tetanus antibodies or tetanus antitoxin. It can be given as intravenous therapy or by intramuscular injection.
2. Antibiotic therapy to reduce toxin production, metronidazole intravenous (IV) is a preferred treatment.
3. Benzodiazepines can be used to control muscle spasms. Options include diazepam and lorazepam, oral or IV.

Severe tetanus:

Severe cases will require ***admission to intensive care***. In addition to the measures listed above for mild tetanus:

Human tetanus immunoglobulin ***injected intrathecally*** (which increases clinical improvement from 4% to 35%)

- Tracheotomy and mechanical ventilation for 3 to 4 weeks. Tracheotomy is recommended for securing the airway because the presence of an endotracheal tube is a stimulus for spasm.
- Magnesium sulfate, as an intravenous infusion, to control spasm and autonomic dysfunction.
- Diazepam as a continuous IV infusion.

Drugs such as diazepam or other muscle relaxants can be given to control the muscle spasms. In extreme cases it may be necessary to paralyze the person with curare-like drugs and use a mechanical ventilator.