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A Review on Leprosy

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Abstract: *Leprosy is a chronic infection caused by the bacterium Mycobacterium leprae. The disease manifests on a clinical spectrum between tuberculoid (strong cell-mediated immunity) and lepromatous (weak immunity, most contagious) poles. Transmission is primarily via aerosolized droplets from untreated, multibacillary patients. Although the WHO declared leprosy "eliminated" globally in 2005 about 250,000 new cases are still reported annually. Diagnosis often relies on the classic clinical sign of a skin patch with reduced sensation, as mycobacterium leprae cannot be cultured. The standard treatment is Multidrug Therapy (MDT), which is highly effective and free worldwide. Paucibacillary (PB) leprosy (1-5 lesions) is treated for 6 months with rifampicin and dapsone, while Multibacillary (MB) leprosy (>5 lesions) is treated for 12 months with rifampicin, dapsone, and clofazimine. Prevention includes chemoprophylaxis for contacts and the BCG vaccine. Key challenges to elimination include the stall in new case numbers since 2006, the reliance on passive case detection, and diagnostic delays caused by stigma, which lead to disability*

Keywords: Leprosy, Mycobacterium leprae, Multidrug Therapy (MDT), Tuberculoid, Lepromatous, BCG Vaccine, Armadillo

I. INTRODUCTION

Hansen's disease, or Leprosy, is caused by a tiny, tricky called Mycobacterium leprae. This organism is an "obligate intracellular" one, which simply means it has to live inside human cells to survive. The disease itself isn't one-size-fits-all; its symptoms fall somewhere on a spectrum between two types: tuberculoid and lepromatous. This depends entirely on how well a patient's immune system fights back against the bacteria. (1)

Before we had effective antibiotics, people who were diagnosed with leprosy were often shunned and isolated from their families and communities. This was out of fear that the condition was highly contagious, even though it's now known to be much less communicable than people once thought. While the World Health Organization (WHO) declared in 2005 that leprosy had been "eliminated" as a global public health problem, new cases are still being reported today. Globally, an average of 250,000 new patients are reported every year. The rate of new cases and the number of people currently being treated varies widely by country. Unfortunately, developing countries carry the heaviest burden of the disease. (2)

History:

Leprosy is an extremely ancient disease that has spread across various global populations over the centuries. Historically, the three major clusters where leprosy was first documented and widespread were India, China, and Egypt. (1)

India (First Medical Description): The first known medical description of the disease was found in an ancient Indian treaty called the Sushruta Samhita, which dates back to 600 BC. China: The first clinical description that appears consistent with leprosy in China dates from the 3rd century BC .India (Physical Evidence): Even earlier, physical evidence was found in India—specifically, four skulls showing lesions characteristic of leprosy were dated to the 2nd century BC. (3)

Scientists found the oldest biological proof of leprosy in a man's skeleton discovered near Jerusalem. This man lived around the 1st century BC (over 2,000 years ago).

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They were able to identify the disease by using molecular biology to isolate the DNA of the leprosy bacteria (M. leprae) from his bones. In short, ancient bones and modern DNA technology were used to confirm the earliest known case of leprosy in a human from the area near Jerusalem. (4)

The DNA of M. leprae (the bacterium that causes leprosy) suggests that it first appeared in Africa. From there, it traveled and spread to other continents, including Asia and South America. (5) 1981: The First Recommended Treatment

WHO officially recommended using a combination of drugs called multidrug therapy (MDT).The therapy generally included: Rifampicin and Dapsone for the milder type of the disease. Rifampicin, Dapsone, and Clofazimine for the more severe type (multibacillary).1995: Treatment Becomes Free Worldwide

A decision was made to ensure that all leprosy patients around the world could receive this multidrug treatment for free. (6)

Leprosy control:

To meet this goal, "elimination" was specifically defined as reducing the number of leprosy cases so that there was less than one case for every 10,000 people in the population.

In short: The WHO decided that if a country could get its leprosy rate down to less than 1 in 10,000 people by the year 2000, they could consider the disease 'eliminated' as a major public health issue. (7) Instead of aiming for the hard-to-achieve, absolute goal of elimination (which usually means a disease is completely gone or at an extremely low level), the focus shifted to reducing the burden.

This phrase, "reducing leprosy burden," is a more humanized way of saying they are working to lessen the overall negative impact of the disease. (8)

The Millennium Development Goals (MDGs) were an agreement made by global leaders at the UN's Millennium Assembly in 2000.

They set out eight main goals to improve global well-being by:

Eliminating extreme poverty and hunger.
Ensuring everyone gets a primary education.
Promoting gender equality and empowering women.
Lowering the death rates of children and mothers.
Fighting major diseases like HIV/AIDS and malaria.
Protecting the environment.
Creating a global partnership to achieve all this.

Essentially, they were a time-bound blueprint for global cooperation to drastically reduce poverty and improve health and education worldwide by 2015. (9)

Pathogenesis

Mycobacterium leprae is a type of acid-fast bacterium that can only survive inside the body. It mainly infects the skin and peripheral nerves, especially in cooler parts of the body such as the chin, cheeks, earlobes, knees, and hands or feet. (22)

Humans are the main reservoir for Mycobacterium leprae. The disease is usually spread by aerosolized droplets from people with lepromatous leprosy and, less commonly, through direct skin contact. Although these are considered the primary routes of transmission, many patients have no identifiable contact with an infected person.

Most people in the world are naturally resistant to leprosy. However, the disease does show familial clustering, and studies of twins demonstrate high concordance rates, suggesting that genetics play an important role in susceptibility. One gene in particular—nramp1—helps regulate susceptibility to mycobacterial infections in mice and appears to influence susceptibility to leprosy in humans as well.

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Genetic factors also help determine the clinical form of leprosy. Certain HLA (human leukocyte antigen) types are associated with specific disease presentations. For example, the HLA-DR3 genotype is more common in tuberculoid leprosy, while HLA-DQ1 or MT1 types are more often seen in lepromatous. (23)

Pathophysiology

Leprosy is most likely transmitted through nasal or sputum secretions. Studies in mice have shown that the respiratory tract may be a possible route for the bacteria to enter the body. Experimental research suggests that the bacilli enter through the respiratory system rather than through the digestive tract or the skin. (24)

No clear pathophysiological model has been established so far because of (i) the insidious nature of the disease, especially during the early stages of infection, (ii) its slow progression, and (iii) the lack of sensitive and specific diagnostic tests for the sub-clinical phase.

Studying the incubation period of leprosy is difficult for these reasons. Reported incubation periods vary widely, including very short periods in young children, such as 3 to 6 months. (25)

Longer incubation periods tend to occur in adults. The details of how latent infection progresses into symptomatic disease are still not fully understood. Observations in American war veterans who had been stationed in endemic regions show that incubation periods can vary widely.

People living in endemic countries are most likely exposed to the bacteria during childhood, and leprosy is often diagnosed many years later. Incubation periods ranged from 2.9 to 5.3 years in patients who developed tuberculoid leprosy, and from 9.3 to 11.6 years in those who developed lepromatous leprosy.

For individuals who spent only short periods of time in endemic areas, determining the exact incubation period is difficult. As a result, gaining a complete understanding of the pathophysiology of leprosy remains challenging. (26)

Factors affecting epidemiology:

Tuberculosis is a much more common infection and causes significant illness. When describing the patterns of leprosy in a population, experts usually focus on certain key features—such as the age of affected people, the type of leprosy they have, their sex, the rate of disability caused by the disease, and the number of cases found in children. (47) Sometimes, it's hard to completely eliminate leprosy. The best way to prevent its spread is to diagnose and treat cases as early as possible. However, countries where leprosy is common often struggle with delays in diagnosis, which can lead to disability. These delays usually happen because healthcare workers do not receive adequate training. (48) Advances in precise complementary techniques can help break the chain of transmission.

Poor housing conditions, close living proximity to an infected person, overcrowding, and an unhealthy diet (malnutrition) all increase the risk of infection. When someone's immunity is weakened—such as in people with HIV—or when they live in rural areas with limited resources, their cell-mediated immunity is reduced. These situations create ideal conditions for infection to occur, whether through respiratory droplets or direct skin-to-skin contact. (47, 48)

Bacteriology

The microbe that causes leprosy was identified in 1873 by a doctor named Gerhard Henrik Armauer Hansen. (10)

The ability to culture M. leprae in vitro is made difficult by its very long doubling time (14 days). For comparison and to put this time in perspective, the doubling time of M. tuberculosis is about 24 hours, and that of Escherichia coli is approximately 20 minutes.

Laboratory research on M. leprae was, and still is, made difficult by that very long doubling time. However, in 1960, Charles C. Shepard proved that the culture of M. leprae could be successfully done by inoculating the bacterium into the footpads of female Swiss mice (white).

In essence: Growing the leprosy-causing bacteria (M. leprae) is hard because it divides extremely slowly (once every 4 days), unlike common lab bacteria (like E. coli) or even its relative (M. tuberculosis). A breakthrough came in 1960 when a scientist figured out how to grow it inside the paws of white mice instead of a petri dish. (11)

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Scientists initially found it difficult to grow (culture) the leprosy-causing bacteria (M. leprae) because its required body temperature is very specific (between 30 ◦ C and 35 ◦ C)

A major breakthrough in studying the disease came in 1971, when Kirchheimer and Storrs showed that they could grow huge numbers of M. leprae by injecting the bacteria into the nine-banded armadillo.

The armadillo is considered a "perfect animal model" because it is highly susceptible to infection by M. leprae.

This ability to grow the bacteria in large amounts allowed scientists to study the disease, develop antibiotic treatments, and identify if the bacteria were resistant to existing antibiotics. (12)

Whole-genome sequencing (a detailed genetic study) of a new species of Mycobacterium (the type of bacteria that causes leprosy) showed two major things:

Ancient Origin of Leprosy Bacteria

The genetic evidence suggests that M. leprae (the main bacterium that causes classic leprosy) split off from its ancestors a very, very long time ago—more than 13.9 million years ago. This means the lineage leading to the leprosy germ is ancient.

Close Relationship Between New Leprosy Agents

The new Mycobacterium species (the one recently studied) is very similar genetically to M. lepromatosis (another bacterium known to cause a severe form of leprosy).

They are so similar that they must have evolved from the same common ancestor.

Isolation in Tuberculoid Leprosy

The new species of bacteria was recently found in patients who have the milder form of the disease, tuberculoid leprosy. It was sometimes found alongside the classic M. leprae, and sometimes it was found alone. (13)

Genetics

Global Clones: DNA sequencing showed that M. leprae strains from all over the world are 99.99% identical. It has hardly changed its DNA over time (due to "reductive evolution").

Small and Simple: Its DNA is small (3.2 Mb) and has a lower G+C content (57.8%) compared to related bacteria like the TB germ (65.6%).

Half of the DNA is Broken: Only half of its genome is made of working genes. The other half consists of non-functional pseudogenes (dead genes) and non-coding regions. M. leprae has more pseudogenes than any other known microorganism.

Hidden Function: Scientists believe these broken genes, though non-functional, might still be important for regulating how the bacteria causes infection and survives inside human cells.

Close Relative: It shares 90% of its working genes with the M. tuberculosis (TB) germ. (1)

M. leprae, the leprosy bacterium, is small and has a shrunken, fragmented DNA (genome) because it has lost many genes for energy production and metabolism. This makes it a highly specialized parasite that depends completely on its host. (14, 15)

The loss of these genes likely caused M. leprae to lose many of its basic survival functions, forcing it to become a parasite that lives inside cells. (16)

Transmission of leprosy

The exact way leprosy spreads is still a mystery. Humans are the main source, but it might sometimes pass from African green monkeys. (17) and Armadillos in Louisiana. (18)

The most contagious form of the disease is Lepromatous Leprosy because patients often carry an enormous number of leprosy bacteria, sometimes up to 7 billion per gram of infected tissue. In 1897, at a congress in Berlin, a researcher named Schaffer demonstrated that the infection could spread through nasal discharge. He asked two infected patients to talk, cough, and sneeze in front of microscope slides for ten minutes, which resulted in the discharge of 10,000 to 10,000,000 bacteria. However, this proof was initially disregarded, and the scientific community continued to believe that leprosy was transmitted only through direct contact. This belief was later overturned in the 1960s when Shepard's

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research once again proved that nasal lesions could lead to the spreading of a very large number of bacilli, supporting the idea of airborne transmission. (19)
Bacilli: Refers to rod-shaped bacteria.
Tens of millions: A very large number, meaning 20 million, 30 million, 40 million, and so on.
Nasal mucosa: The moist inner lining of the nose.
Discharged: Simply means released or expelled. (20)

It's still unclear how much genetic predisposition contributes to the development of leprosy. Some research suggests that genes involved in the NOD2-mediated signaling pathway—which helps regulate the innate immune response—may play a role. Several candidate genes linked to leprosy susceptibility have been proposed, but confirming these findings has been challenging.
A genome-wide association study comparing leprosy patients with healthy controls has identified new genetic variants associated with both the risk of developing leprosy and the form the disease takes. (21)

Immunology
Immunology plays a major role in leprosy because the body's immune response determines how the disease appears and progresses. When a person's immune system is weakened, they can develop the most severe forms of leprosy. The type of clinical symptoms a patient shows is closely linked to the strength and type of their immune response.
In tuberculoid leprosy, the body mounts a strong cell-mediated (Th1) immune response. This strong response helps control the bacteria, limiting the disease to a few well-defined skin lesions and localized nerve damage. In this form, there is little to no antibody (humoral) response.
In contrast, lepromatous leprosy occurs when the cell-mediated immune response is very weak. Instead, the body shows a mainly humoral (Th2) response, producing large amounts of IgG and IgM antibodies—yet these antibodies are not effective at controlling the bacteria. This weak cellular response allows Mycobacterium leprae to multiply freely, leading to widespread diseaseLeprosy can occur at any age, but most patients become infected in childhood. Many people who live in areas where leprosy is common are exposed early in life, yet most do not develop the disease, even after long-term contact with M. leprae, because their immune system is strong enough to control the infection. (27)

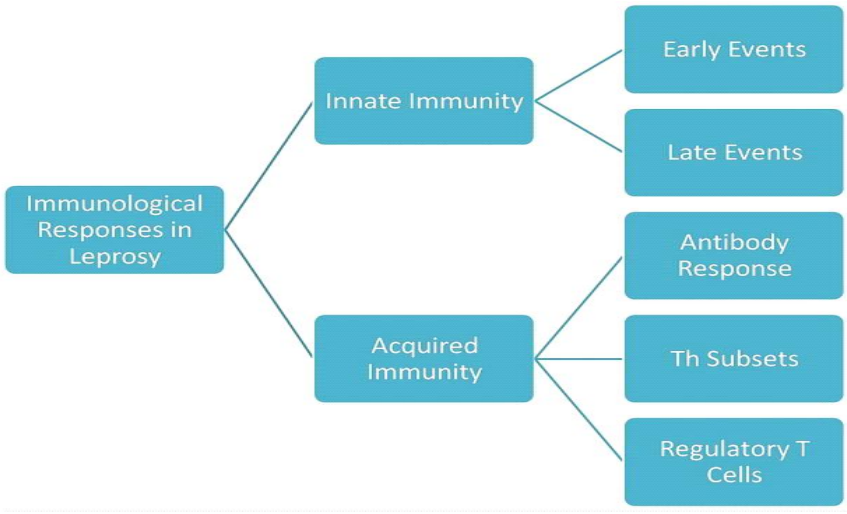

Fig. No. 2 Immunological responses in leprosy

12. Clinical signs
Leprosy is a chronic disease that usually does not cause life-threatening problems right away. Mycobacterium leprae mainly targets the skin and the Schwann cells of peripheral nerves.

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Early on, patients often notice sensory loss due to nerve involvement. If the disease is not treated and patients seek medical care at a later stage, more severe motor problems can develop.

Common complications include plantar ulcers, bone destruction (such as in the nose or fingers), and paralysis—especially of nerves like the ulnar nerve. Eye problems such as lagophthalmos (inability to fully close the eyelids) may also occur.

These complications shape the clinical picture of leprosy, which has been recognized and described for centuries. (28)

In the early stages of leprosy, the symptoms can vary a lot, which makes the disease hard to diagnose. Traditionally, cases were grouped into two main types: tuberculoid leprosy and lepromatous leprosy. However, many patients show symptoms that fall somewhere between these two extremes. These in-between forms are called borderline (or intermediate) leprosy.

To make sense of all these different presentations, the Ridley and Jopling (RJ) classification system was developed. It places patients along a spectrum between tuberculoid and lepromatous forms, depending on their clinical features and immune response. (29)

There are five main clinical presentations of leprosy (see Fig. 2).

13. Classification

To simplify treatment decisions, the WHO recently introduced a new classification system.

Traditionally, leprosy has been classified along a spectrum with five types:

T (Tuberculoid leprosy – polar tuberculoid)

BT (Borderline tuberculoid)

BB (Borderline borderline)

BL (Borderline lepromatous)

LL (Lepromatous leprosy – polar lepromatous)

The WHO system groups these forms into two practical categories:

Paucibacillary (PB) leprosy

Defined as having 1 to 5 skin lesions and/or one damaged peripheral nerve.

Multibacillary (MB) leprosy

Defined as having more than 5 skin lesions or more than one damaged nerve.

This simplified system helps make treatment choices easier and more standardized worldwide. (29)

Leprosy can appear in different forms depending on how strong a person's immune system is against the bacteria Mycobacterium leprae. The disease exists on a spectrum, from tuberculoid leprosy (strong immunity) to lepromatous leprosy (weak immunity). In between these two extremes are the borderline forms.

Tuberculoid Leprosy

Few skin lesions, usually pale patches with clear borders.

These areas often have reduced or lost sensation.

Lesions may be slightly thickened.

Nerve damage occurs near the lesions, causing sensory or motor problems, especially in hands and feet.

Lepromatous Leprosy

Many lesions (often 20–100), appearing symmetrically on both sides of the body.

Lesions are found especially on the face, earlobes, fingers, and toes.

They can be papules or nodules (called lepromas), copper-colored.

Widespread, symmetrical nerve damage is common.

Borderline Leprosy

Borderline types fall between tuberculoid and lepromatous.

Borderline Tuberculoid (BT)

Asymmetrical, few lesions

Reduced sensation

Some nerve enlargement and nerve damage

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Borderline Borderline (BB)
Multiple annular (ring-shaped) lesions with indistinct edges
Smaller lesions appear around bigger ones Not fully anesthetic

Borderline Lepromatous (BL)
More than 10 lesions, usually bilateral Lesions are not anestheticLeans toward the lepromatous end with diffuse nerve damage. (31)

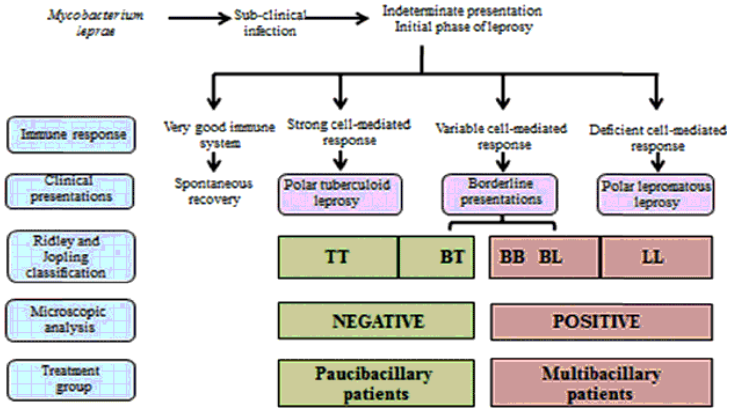

Fig. No. 3: Clinical, biological, and therapeutic classification of leprosy (1)

Risk factors

Leprosy is more common in communities with poverty and lower socioeconomic conditions, but there are no special additional risk factors beyond that. Unlike tuberculosis, leprosy does not show any link with other infectious diseases such as HIV. In other words, the frequency of leprosy does not rise or fall together with HIV or other infections. (32)
Some people may be genetically more prone to getting leprosy, but only a few of the suspected risk-related genes have actually been confirmed in large studies across different populations. In other words, while many genes have been proposed to increase a person's susceptibility, only a small number have been reliably validated. (33)
Among the genes that can increase the risk of developing leprosy, one example is a region on chromosome 6 that controls the activity of two genes: PARK2 and PACRG (Parkin co-regulated gene). The exact role of the PACRG gene is still unknown. The PARK2 gene, however, is known to be involved in one of the cell's protein-degradation systems (the ubiquitination pathway) and is also linked to Parkinson's disease. Variations in this chromosome region are associated with certain clinical forms of leprosy. (34)

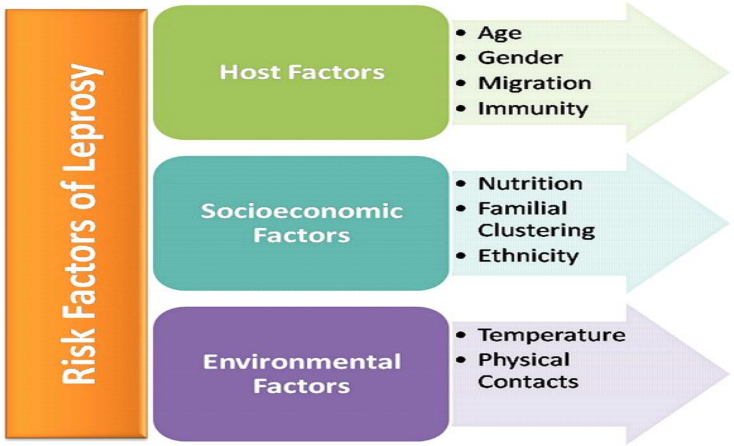

Fig. No. 4: Risk factors affecting leprosy

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Treatment

The WHO recommends multidrug therapy (MDT) for leprosy. For Paucibacillary leprosy, the standard treatment is rifampicin and dapsone for 6 months. For multi bacillary leprosy, patients should receive rifampicin, dapsone, and clofazimine for 12 months. (35) According to the WHO Technical Advisory Group (2009), this treatment effectively kills M. leprae in most patients. They also noted that people are unlikely to remain infectious after starting MDT. In some cases—especially in patients who have a high bacterial index at diagnosis—a longer course of treatment might be needed to prevent relapse. There is an ongoing clinical trial comparing different treatment durations for multi bacillary leprosy. Overall, in terms of public health, the recommended MDT regimens are considered reasonable and effective. (36)

People with the lepromatous, multibacillary form of leprosy are the main source of M. leprae in the community. If these patients relapse after treatment, they can start spreading the bacteria again, which makes relapse an important public-health concern. The relapse rate after multidrug therapy (MDT) varies between studies because of differences in how long patients are followed and how relapse is defined. However, most data show that relapse rates stay below 2–3 cases per 100 person-years. Certain factors increase the risk of relapse, such as receiving monotherapy in the past, incomplete or irregular treatment, having many skin lesions or thickened nerves, and not showing a good response to treatment. To correctly diagnose a relapse, doctors need to look at clinical signs, bacteriological tests, and treatment history. A skin biopsy (histopathology) can be useful, but it isn't always available in routine practice. Additionally, patients with lepromatous leprosy usually do not react to the lepromin skin test. (35)

Accurately diagnosing a relapse of leprosy requires looking at several things together: the patient's symptoms, laboratory tests, and how they responded to previous treatment. A biopsy (histopathology) can help, but it's often not available in many places.Both a true relapse and a type 1 immune reaction can cause new skin lesions and worsening nerve damage, which makes it harder to tell them apart. (36) According to current WHO guidelines, multidrug therapy should only be restarted when a relapse is clearly confirmed. Drug resistance in Mycobacterium leprae is still uncommon. In the rare cases where resistance is suspected, most patients have responded well to being treated again with rifampicin, dapsone, and clofazimine. (37)

Testing whether M. leprae is resistant to treatment was traditionally done by injecting tissue from a patient's biopsy into the footpads of mice and then checking if the bacteria grew. Today, this method is supported by DNA sequencing, which looks for specific gene mutations known to cause resistance to rifampicin, ofloxacin, and dapsone. Several resistance-related genes have already been identified, although we still don't fully understand how important each of these mutations is in clinical practice. A global surveillance program has been established to monitor drug-resistant leprosy. The WHO's Technical Advisory Group has encouraged expanding this work in selected countries. Although multidrug therapy has been highly successful, no new antibiotics for leprosy are currently available, making it important to strengthen research efforts in drug screening, experimental treatments, and clinical trials. More capacity is needed in these areas to rebuild expertise that has been lost over time and to develop alternative treatment options for the future. (36) M. leprae, like other mycobacteria, is naturally resistant to many commonly used antibiotics.

This resistance comes from the thick, lipid-rich cell wall of the bacterium, which makes it difficult for antibiotics—especially hydrophilic ones like β-lactams, glycopeptides, fusidic acid, and chloramphenicol—to enter the cell.Before modern treatments were discovered, chaulmoogra oil, extracted from the fruit of the Hydnocarpus kurzii tree, was the first therapy used for leprosy. Some compounds in this oil work against certain mycobacteria, but they are not effective against M. leprae. (38)

Second-line antibiotic

such as fluoroquinolones (ofloxacin, levofloxacin, and moxifloxacin), minocycline, and clarithromycin—are used when first-line drugs like rifampicin cannot be given. This may be because the patient cannot tolerate them, has rifampicin-resistant leprosy, or the treatment has failed.These antibiotics have broad activity against both gram-positive and gram-negative bacteria, but they are less bactericidal than rifampicin, meaning they kill the bacteria more slowly.

Because of this weaker effect, patients with rifampicin-resistant leprosy need to take these medicines every day, and the treatment duration must be extended to about 4 months. Despite being less potent than rifampicin, these drugs provide valuable therapeutic alternatives when first-line options cannot be used. (39)

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New therapeutic approaches are being developed.

Bedaquiline, a Diarylquinoline also known as 207910 or R207910 (MC207), is a newer tuberculosis drug that works by inhibiting ATP synthase. Its bactericidal (bacteria-killing) effect against M. leprae in mouse studies is similar to that of ofloxacin and rifampicin.At the moment, there are very few new drugs that work against M. leprae. Bedaquiline has not yet been tested in patients with leprosy. (1)

Diagnosis

Delays in diagnosing leprosy can happen for two main reasons: patients may take a long time to seek medical help, and health services may take time to recognize the disease. The reasons why patients delay going to a clinic differ from place to place, but stigma often plays an important role. When diagnosis is late, the infection continues to spread and the chances of developing disabilities increase. Several factors can contribute to late diagnosis. (40)

Clinical Diagnosis

In most cases—about 90%—leprosy is identified through skin changes. Skin patches that have reduced sensation (numbness) are usually the main sign of the disease, and this is especially important if the person lives in, or has lived in, a region where leprosy is common. These numb skin lesions are considered the "classic" sign because no other skin condition presents exactly like this.The remaining 10% of patients may not show obvious skin changes but instead have nerve-related symptoms, such as numbness, tingling, or weakness. A patient's medical history—particularly their symptoms and where they have lived—is often the first clue in identifying leprosy, since the disease is closely linked to sensory loss caused by nerve involvement. (41)

To diagnose leprosy properly, a specialist needs to carefully examine the patient's skin patches and nerve damage. This helps determine how severe the disease is, how infectious the patient might be, and whether there is a risk of developing reversal (immune) reactions.

Whenever possible, additional tests—such as microbiological and pathological examinations—should be done to support the clinical diagnosis. These tests are usually done on a skin biopsy or, when the patient mainly shows nerve problems, on a nerve biopsy. The results help confirm the diagnosis and classify the disease using both the Ridley–Jopling (RJ) and WHO systems.

This classification is important because it guides the choice of the right treatment and helps predict how the disease may progress.

Microscopic analysis and acid-fast bacilli.

Since Mycobacterium leprae cannot be grown in the lab, the standard method for detecting it is to look for acid-fast bacilli under a microscope. (29)

Pathological diagnosis

To diagnose leprosy, doctors examine a skin biopsy.

In lepromatous leprosy, the biopsy shows many "foamy" cells (Virchow's cells). These gather around hair follicles, sweat glands, and small nerves without entering them. The infiltration can damage tiny nerves and sweat glands, causing numbness in the skin. A clear layer called Unna's band separates the affected area from the upper skin.In tuberculoid leprosy, the biopsy shows tight clusters of immune cells around hair follicles, glands, and nerves. This inflammation often leads to nerve damage and loss of sensation. (42)

Immunological diagnosis

When someone is infected with M. leprae, their body produces a mix of immune responses, including antibodies that unfortunately don't provide real protection. One of the key molecules on the surface of M. leprae is called phenolic glycolipid-1 (PGL-1).Researchers have studied PGL-1 to develop diagnostic tests for leprosy. Many population studies have used a specific blood test that looks for IgM antibodies against PGL-1. More recently, newer tests have been created that can detect both IgM antibodies against PGL-1 and IgG antibodies against another M. leprae–specific protein called LID-1 (a fusion protein). (43)

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Prevention

Household Contacts: Chemoprophylaxis (preventive antibiotic treatment) significantly reduces the chance of developing leprosy among people living in the same household as a patient.

General Population Debate: Experts are still debating whether to use this strategy more broadly in the general population.

Rifampicin Effectiveness (Single Dose): A single dose of rifampicin can prevent the disease from developing in people who are already infected.

Rifampicin Limitation: This treatment is most effective for individuals who are not close contacts and who have very low levels of the Mycobacterium leprae bacteria. (44)

Concern: Doctors worry that using only one drug (monotherapy) could lead to antibiotic resistance.

Recommendation: Experts recommend a short combination treatment instead.

Dosing: This treatment involves one or two doses of three medicines taken together.

The Three Medicines and Dosages:

Rifampicin: 600 mg

Ofloxacin: 400 mg

Minocycline: 100 mg (40)

Using this treatment plan would be much more expensive.

Evidence vs. Practice: There is strong epidemiological evidence to support giving preventive medicine to close household contacts, but implementation is complicated.

Need for Disclosure: Implementation requires openly identifying and informing others that someone in the household has leprosy.

Privacy/Ethics Concerns (Household): This disclosure can be unwanted, uncomfortable, or unethical in certain situations.

Extending to Non-Household Contacts: Giving prophylaxis to close contacts who don't live in the same home raises even more challenges.

Difficulty in Identification: Finding and identifying these external contacts can be very difficult.

Wider Privacy Concerns: The process of tracking external contacts could create privacy concerns or social problems. (44)

The current For Further Reducing the Disease Burden due to Recommendation in WHO's Enhanced Global Strategy Leprosy disease. (45)

If no preventive medicine is used, it becomes even more important to teach close contacts how to recognize early signs of leprosy and to come back for evaluation if any symptoms appear.

Recommendations & BCG Vaccine

WHO Recommendations (Chemoprophylaxis)

BCG Vaccine (Tuberculosis/Leprosy)

Dual Protection: The BCG vaccine (primarily for tuberculosis) also offers some protection against leprosy.

Impact: Giving BCG to newborns has likely contributed to the reduction in leprosy cases in many areas.

Contraindication: BCG is a live vaccine and must not be given to people infected with HIV.

The level of protection BCG provides against leprosy varies between different populations.

Scientists do not fully understand the reason for this difference in efficacy.

Research and Funding Issues :

Lack of Ideal Animal Model: Mice don't develop the disease like humans; armadillos are useful but not ideal or widely available.

Low Priority/Funding: Leprosy is less common than tuberculosis (TB), resulting in less attention and funding, despite being caused by related bacteria.

Impact of Tuberculosis (TB) Research :

Focus on TB Vaccines: Most new research focuses on future TB vaccines to replace the current BCG vaccine.

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Loss of BCG Protection: Replacing BCG may cause a loss of its partial protection against leprosy, unless the new TB vaccines also protect against it.
Shared Immune Understanding: Understanding the immune response to mycobacterial infections could help improve both TB and leprosy vaccines.
Dual-Purpose Vaccine Potential: It might be possible to design a new TB vaccine that includes added protection against leprosy.
Economic and Scientific Context
Cost-Effectiveness: Developing a leprosy vaccine is not considered cost-effective due to the gradually decreasing global number of cases.
New Opportunities: Advances like the full genetic sequencing of Mycobacterium leprae have opened new opportunities for vaccine development. (46)

Leprosy: the future
Challenges in Leprosy Elimination
Long-term goal: Eliminating leprosy worldwide.
Major issue: Passive detection of cases.
Health systems wait for individuals to show symptoms (patient-initiated).
Traditional/Common Public Health Approach:
Educate communities on leprosy signs.
Depend on individuals to seek medical care after noticing symptoms.
Current Reality: This passive approach is still common even in areas with high leprosy prevalence. (49)
Multidrug Therapy (MDT): Has reduced the number of people currently living with leprosy (prevalence).
Problem: The number of new cases reported each year (incidence) has not changed much.
Reason: MDT does not significantly stop the spread of leprosy, particularly within households.
(Treatment cures the patient but does not prevent transmission to close contacts.) (50)
High-risk groups (e.g., close contacts of patients) are targeted.
Preventive medicines (like rifampin or dapsone) have been used.
This prophylactic approach has not been very successful. (51)
Actually, the only preventive measure that has shown real success is the BCG vaccine (bacille Camille-Guérin).
A single dose of this vaccine gives about 50% protection against leprosy." (52,53)
Continued Global Existence: Leprosy will persist in countries with poor detection/treatment.
Increased Global Travel: Leads to occasional cases being imported to Canada from abroad.
Canadian Health-Care Need: Providers must recognize signs and manage leprosy.
Barriers to Diagnosis & Treatment:
Delays in seeking medical care.
Language barriers.
Low socioeconomic status.
Stigma associated with leprosy in some communities.
Immigration process can fragment care, leading to inconsistent evaluation/treatment. (54)
A lack of awareness about leprosy often leads to missed or incorrect diagnoses. If the disease isn't recognized and treated early, it can cause serious long-term nerve damage. Even though leprosy is rare, it is curable when proper medications and follow-up care are given.
Because of this, healthcare providers should keep leprosy in mind when evaluating patients who have long-lasting skin rashes or nerve problems—especially if they have spent a long time in, or previously lived in, countries where leprosy is more common.If leprosy is suspected, the patient should be referred quickly to a specialist who has experience treating the disease. (55)

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