

Basic Insights into Lymphatic Filariasis



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ABSTRACT

Lymphatic filariais, a debilitating disease which is caused by parasitic worms and transmits by bite of a mosquito. The epidemiology of the disease refers to the certain environment conditions which promote the breeding of mosquitos' carrying the LF disease. There is High risk population and socioeconomic impacts that have increased the prevalence of the disease to certain regions. It is also associated with the spread of causative agents which shows persistence in topical and subtropical regions. Moreover, the burden of disease due to lack of treatment opportunities is much dense in regions like India and Nigeria. The disease is neglected yet complex due to reciprocity between humans and mosquitos. The morphology circulates around the injection of the microfilariae by mosquito from blood meal, developing infection causing larvae and again transmits to human but a new one this time. The understanding of transmission dynamics of LF is a key step to address disease precisely. However, in mosquito microfilariae undergoes several life stages and after the L3 stage it penetrates to human lymphatic system. The pathogenicity of LF can be assessed by host parasite interaction and certain immune responses. The recognition of parasite as an antigen stimulates innate immune system, T cell activation linked with APC's. but if the LF infection replicates it causes severe stages of LF. Lymphedema caused by chronic infection in worst cases can lead to disability. Hydrocele, lymphangitis and elephantitis are the hallmark of clinical manifestation predilection debility of lymphatic system.

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1. INTRODUCTION

1.1. LYMPHATIC FILARIASIS; INSIGHT TOWARDS ITS ETIOLOGY

Lymphatic filariasis, also known as elephantiasis, is a parasitic disease caused by thread-like filarial worms that belong to the nematode family. Being a vector-borne disease, Lymphatic filariasis refers to an infection causing which is mostly neglected all over the world. Lymphatic filariasis is transmitted through the bite of infected female mosquitoes, from the genera Culex, Anopheles, and Aedes. The nematodes which are the real cause of the disease are passed on through mosquitos. Humans become hosts for the vectors, but the adult worms still do not multiply in humans. That is why tourists and travelers exposed to the infection are shortly affected, and it persists for a short time. However, children are more prone to get the transmission, and pervasiveness gets more with age.

These parasites are transmitted to humans by mosquito biting and the human gets infected. The worm at this point is only 1mm in length. The larvae then travel to the lymphatic vessels of the human and transform within 9 months with 7-10cm in length. for the areas in which the mosquitos have maximum activity at night, the larvae have many possibilities to be detected in the bloodstream during the night and vice versa for areas with maximum activity in the daytime. The microfilariae in blood are ingested by mosquitoes while the mosquito takes human blood as a meal. Microfilariae penetrates the midgut of the mosquito and develops itself into L1 larvae. The L1 larvae develop into L3 larvae which are again transmitted to humans through mosquito biting. By the source of this whole life cycle, the repeated bits of mosquitoes spread lymphatic filariasis to humans. Filariasis is much influenced and dependent on the time of exposure to mosquito bites. And also depends on the presence of antigens of adult worms in vessels.

However, the detection of the microfilaria is done blood microscopy. It can also be done by detecting filarial antigen in blood using molecular technique like ELISA or by detecting the filarial DNA using the techniques like PCR. The most preferable technique is detecting the antigen in the blood through ELISA because it doesn't specify the timings of taking blood sample and it's easy to run. The adult worms can also be detected using ultrasonography. As the adult worms are distinguishable because of their sizes or quick or so-called dancing movements with is different from other blood movement.

2. EPIDEMIOLOGY OF LYMPHATIC FILARIASIS

Region	Frequency level	Endemicity	
East Asia	Low	Occasional	
Oceania	Moderate	Regional	
Southeast Asia	Moderate	Regional	
South Asia	High	Common	
Pacific Islands	High	Common	
Central America	Low	Occasional	
Europe	Negligible	Eradicated	

Geographical Distribution:



In Asia, *Lymphatic filariasis* was widely spread in some areas of Southeast Asia, and the Western Pacific region. India and Bangladesh are marked with a very high frequency of Lymphatic filariasis. While China is less endemic, in America, Lymphatic filariasis was widely spread in some areas of the Caribbean and South America (Michael et al. 1996).

Not very common in regions of Europe. Rural areas suffer more from Lymphatic filariasis because of poor health and un-hygienic condition in those areas.

2.1. HIGH-RISK POPULATIONS AND SOCIOECONOMIC IMPACT

Lymphatic filariasis has mostly affected the tropical and subtropical regions. As such tropical and subtropical areas provide more favorable climatic circumstances for pests to spread the disease, and Lymphatic filariasis is likely to occur there more frequently (Ottesen 2006) Areas with more density of mosquitos are at more risk of Lymphatic filariasis transmission as the mosquitos transfer their contaminated maggots from one carrier to another person. Another reason could be thatun-hygienic sites and bad conditions of places can initiate the rookery for mosquitos that could be very favorable for the transmission of disease. Another big reason is when infected persons move from one place to another, they transmit disease to the healthy person another reason could be poverty. (Ramaiah et al. 2000).

LF can have different indirect effects on individuals' health and socioeconomic factors. For example, *Lymphatic filariasis* can affect different body parts like the limbs which cause them to be swollen and this eventually reduces the working abilities and activities of a person which effects overall community. As children with disease cannot attend schools because of their health and also because of the risk of transmitting the disease, so it largely affects their education and their future career (Shenoy et al. 2009). When the infected bread earner couldn't go outside for earning, the house income will be very low and this could lead towards poverty. Infected people will not be able to attain enough education which causes less social climbing and ultimately no growth of the society. LF will cause major effect on the industries. The people who are infected and have any disability or abnormal body part have a high possibility of being victimized and discriminated, they will separate themselves from other people shrinking their social circle and life (Mak 2007).

2.2. BURDEN OF DISEASE

The number of cases of Lymphatic filariasis vary from time to time because of the amount and type of treatments, betterment of monitoring of the disease and different other factors. It is an estimate that around one-twenty million population was infected due to this disease *Lymphatic filariasis* and about a billion people were endangered of being infected with the disease in 80 countries.(Edeson et al. 1960) It is thought that India was in the no.1 in the list of infected countries, followed by Nigeria which was on the no.2 with most infected LF patients. Other regions included, South America, Africa and Western Pacific sides. Mass Drug Administration is being applied in many regions of Ghana. (Gyapong et al. 1996).

Wuchereria bancrofti, Brugia malayi and *Brugia timori* are the three filariasis responsible for the disease Lymphatic filariasis. *Wuchereria bancrofti* caused about 90% of the LF cases and the second two filariasis caused around 10% of cases (de Souza et al. 2014).

2.3. DISABILITY-ADJUSTED LIFE YEARS (DALYs)

Is a measure used to estimate the life lost in deaths, any type of disability or in bad health conditions. As Lymphatic filariasis can lead to many health abnormalities like disabilities of body parts or specifically Elephantiasis, which reduces the life expectancy of individuals, losing their

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DALY's. Different health policies and measures are changed as WHO monitors the risks of Lymphatic filariasis and evaluate their DALY's (Addiss et al. 2000).

3. PARASITE BIOLOGY AND LIFE CYCLE

3.1. TYPES OF FILARIAL PARASITES INVOLVED

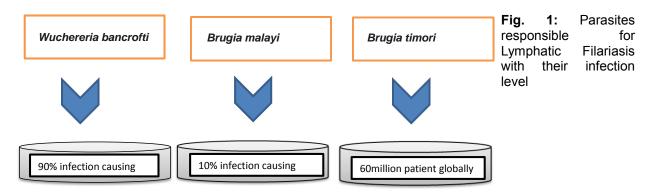
The filarial parasites mentioned in lymphatic filariasisare mentioned below in Fig. 1. (Paily et al. 2009).

3.1.1. WUCHERERIA BANCROFTI

This is the most common and widespread filarial parasite responsible for causing lymphatic filariasis in humans. It is primarily found in tropical and subtropical regions of Africa, Asia, the Pacific Islands, and parts of the Americas.

3.1.2. Brugia malayi

Another important filarial parasite that causes lymphatic filariasis, primarily found in Southeast Asia and parts of the Western Pacific.



3.1.3. Brugia timori

Similar to *Brugia malayi*, this filarial parasite also causes lymphatic filariasis, primarily found in certain regions of Southeast Asia (Babu and Nutman 2014).

3.2. MORPHOLOGY AND LIFE STAGES OF THE PARASITES

The filarial parasites have a complex life cycle that involves multiple stages, both in the human host and the mosquito vector as mentioned in Fig. 2. (Cheng 1973). The key life stages of filarial parasites are as follows:

3.2.1. MICROFILARIAE

These are the first-stage larvae of the filarial parasites. *Microfilaria*e are tiny, elongated, and thread-like, measuring about 200 to 300 micrometers in length. They circulate in the bloodstream and lymphatic system of the infected human host (Famakinde 2018). **3.2.2. MOSQUITO STAGE**



When an infected mosquito of the appropriate species feeds on a human, it ingests the microfilariae along with the blood.

3.2.3. L1 STAGE

Inside the mosquito, the microfilariae shed their sheaths and penetrate the mosquito's gut, becoming first-stage larvae or L1.

3.2.4. L2 STAGE

Over the course of about one to two weeks, the L1 larvae molt into the second-stage larvae or L2.

3.2.5. L3 STAGE

After further development (approximately one to two weeks), the L2 larvae molt into the infective third-stage larvae or L3. These L3 larvae migrate to the mosquito's proboscis (mouthparts), ready to be transmitted to the next human host.(Lawrence and Devaney 2001).

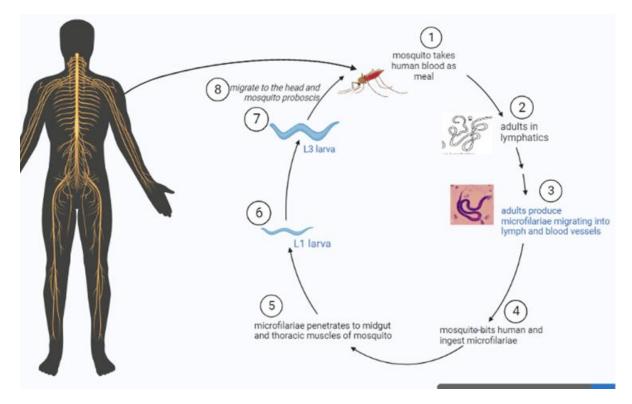


Fig. 2: Life stages of Filarial Worm CDC)

3.2.6. HUMAN STAGE

When an infected mosquito takes a blood meal from a human, it deposits the infective L3 larvae onto the skin.



3.2.7. L3 TO L4 MOLT

The L3 larvae penetrate the bite wound and enter the human host, where they continue to migrate through the subcutaneous tissues. Over several days, the L3 larvae molt into the fourth-stage larvae or L4.

3.2.8. L4 TO ADULT MOLT

The L4 larvae continue to migrate, typically reaching the lymphatic vessels and lymph nodes. There, they molt into immature adults and then further into sexually mature adult filarial worms (Roberts et al. 2009).

3.2.9. ADULT STAGE

The adult filarial worms reside in the lymphatic vessels and lymph nodes of the human host, where they mate and produce microfilariae, completing the life cycle (Wilke and Marrelli 2015).

3.3. TRANSMISSION MECHANISMS (MOSQUITO VECTORS) OF LYMPHATIC FILARIASIS

> Lymphatic filariasis is transmitted through the bites of infected mosquitoes, which act as vectors for the filarial parasites. The main mosquito species involved in the transmission of *Wuchereria bancrofti, Brugia malayi,* and *Brugia timori* are usually from the genera Culex, Anopheles, and Aedes.

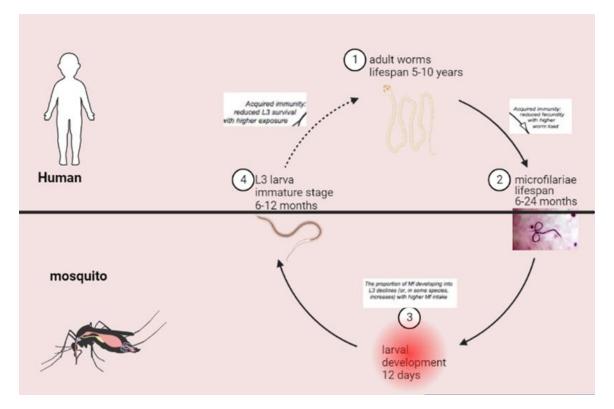


Fig. 3: Cycle of transmission for LF. It shows W. bancrofti life cycle. Microfilariae live in lymphatic system for 5-10 years. Female worms reproduce many MF in blood living for 6-24 months. L3 develops inside



mosquitoes in 12 days and can cause infection in humans. While mosquito take other bite L3 is transmitted to the human body migrating to blood and lymphatic system. This immature period takes 6-12 months. And grows to mature adult worms.

> The transmission cycle begins when an infected mosquito takes a blood meal from a human already infected with adult filarial worms. During the blood meal, the mosquito ingests the microfilariae that circulate in the bloodstream and lymphatic system of the human host (Cheng 1973; Amuzu et al. 2010).

➤ Inside the mosquito, the microfilariae go through several larval stages (L1 to L3) and become infective third-stage larvae (L3) in the mosquito's proboscis. When the mosquito feeds again, it deposits these infective L3 larvae onto the skin of another human, usually during its nighttime feeding activities (Witt and Ottesen 2001).

> The L3 larvae penetrate the skin through the bite wound created by the mosquito and then migrate through the subcutaneous tissues. Eventually, they reach the lymphatic vessels and lymph nodes, where they mature into adult worms, continuing the cycle of infection (Day 1991).

➢ It is important to note that not all mosquito species are capable of transmitting filarial parasites as mentioned in Fig. 3, and the transmission dynamics can vary depending on the geographical region and specific mosquito vectors involved. Controlling the mosquito population and preventing mosquito bites are essential strategies for controlling and preventing lymphatic filariasis. Mass drug administration of antifilarial drugs to affected communities is also used to reduce the number of microfilariae in the human population, thereby decreasing the transmission potential (Stolk et al. 2015).

3.4. SIGNALING PATHWAY OF LYMPHATIC FILARIASIS

Lymphatic filariasis, commonly known as elephantiasis, is a parasitic disease caused by threadlike worms called filarial nematodes, mainly *Wuchereria bancrofti, Brugia malayi*, and Brugia *timori*. These worms are transmitted to humans through the bites of infected mosquitoes.

The signaling pathways involved in lymphatic filariasis primarily revolve around the host's immune response to the presence of the filarial worms and their antigens. When the mosquito bites and deposits the infective larvae into the human host, they migrate through the lymphatic vessels and develop into adult worms that live within the lymphatic system.

Here is an overview of the signaling pathway and immune response in lymphatic filariasis:

3.4.1. RECOGNITION OF PARASITE ANTIGENS

The immune response begins with the recognition of filarial antigens by the host's innate immune system. These antigens can be derived from the parasites themselves or released from their dead or dying cells.

3.4.2. ACTIVATION OF INNATE IMMUNE CELLS

Dendritic cells, macrophages, and other antigen-presenting cells (APCs) are crucial in detecting and capturing the filarial antigens. Once they engulf the antigens, they process and present them on their cell surfaces using major histocompatibility complex (MHC) molecules (Sreenivas et al. 2017).

3.4.3. ANTIGEN PRESENTATION AND T CELL ACTIVATION

The APCs then migrate to lymph nodes where they present the filarial antigens to T cells. This presentation activates CD4+ T helper cells, which play a central role in orchestrating the immune response.



3.4.4. TH1 AND TH2 RESPONSE

Lymphatic filariasis triggers a complex balance between two types of T helper cells: Th1 and Th2. Th1 cells produce pro-inflammatory cytokines like interferon-gamma (IFN-gamma) that activate macrophages to kill parasites. Th2 cells produce anti-inflammatory cytokines like interleukin-4 (IL-4) and interleukin-13 (IL-13) that stimulate B cells to produce antibodies (Babu et al. 2005).

3.4.5. ANTIBODY PRODUCTION

The activation of Th2 cells leads to the production of specific antibodies, particularly IgG4 and IgE, against filarial antigens. These antibodies may not directly kill the parasites but are believed to facilitate their elimination by other immune cells.

3.4.6. GRANULOMA FORMATION

Chronic infection with filarial worms can lead to the formation of granulomas, which are aggregates of immune cells around the parasites. Granulomas are an attempt by the immune system to contain the infection and limit its spread (Chakraborty et al. 2013).

3.4.7. REGULATORY T CELLS (TREGS) AND IMMUNE SUPPRESSION

The filarial parasites have developed strategies to evade the host's immune response. They induce the production of regulatory T cells (Tregs) that help dampen the immune response and create an immunosuppressive environment, allowing the parasites to persist (Babu et al. 2006).

3.4.8. LYMPHATIC DAMAGE AND ELEPHANTIASIS

Long-term infection and chronic inflammation can cause damage to the lymphatic vessels. This damage, along with the accumulation of fluid and immune cells, can lead to the development of lymphedema, swelling of limbs, and in severe cases, elephantiasis.

It's important to note that the immune response in lymphatic filariasis is complex and varies from person to person. Some individuals may be more susceptible to severe disease, while others may have a milder course of infection. Additionally, treatments for lymphatic filariasis often focus on antiparasitic medications and managing the associated symptoms such as lymphedema (Edeson et al. 1960).

4. CLINICAL MANIFESTATIONS

Elephantiasis, or Lymphatic filariasis, is a parasitic condition brought on by an infection with filarial parasites, which are worm-like parasites. The primary culprits behind the disease are three species of worms: *Brugia timori*, *Wuchereria bancrofti*, and *Malaysian brugia*. Humans contract the illness from mosquito bites that have been contaminated (Dreyer et al. 2000).

Once the parasites enter the human body through mosquito bites, they migrate to the lymphatic system, which is in charge of preserving fluid balance and warding off infections. In the lymphatic system, the adult worms produce microfilariae, which are tiny, immature forms of the parasites. The microfilariae then circulate in the bloodstream and are taken up by mosquitoes when they bite an infected person, completing the life cycle (Rajan and Gundlapalli 1997).

Lymphatic filariasis can manifest in different ways, depending on the stage of the infection. In the early stages, most individuals remain asymptomatic, but they still contribute to the transmission of the disease (WHO 2013).



4.1. ASYMPTOMATIC PHASE

Many infected individuals do not show any immediate symptoms. This phase can last for years, during which microfilariae can be found in the blood when tested (Mak 2012).

4.2. ACUTE PHASE

In some cases, people may experience acute attacks of lymphangitis, which is inflammation of the lymphatic vessels. This can cause symptoms such as fever, pain, and swelling in the affected limbs or body parts.

4.3. CHRONIC PHASE

Over time, chronic inflammation of the lymphatic vessels and lymph nodes can occur. This leads to the characteristic symptoms of lymphatic filariasis, (Partono 2007) such as:

4.4. LYMPHEDEMA

Swelling of limbs (usually the legs or, less commonly, the arms) due to the accumulation of fluid and blocked lymphatic vessels.

4.5. ELEPHANTIASIS

A severe form of lymphedema where the affected limbs or body parts become extremely enlarged and thickened, resembling an elephant's skin.

4.6. HYDROCELE

Fluid accumulation in the scrotum (in males) or labia major (in females) due to lymphatic obstruction.

4.7. PREVENTION AND TREATMENT

Lymphatic filariasis prevention involves controlling mosquito populations, using insecticidetreated bed nets and indoor residual spraying and using mass drug administration programs to provide antifilarial medications to at-risk populations.

Lymphatic filariasis treatment focuses on managing symptoms and preventing complications. Anti-inflammatory medications are used for acute attacks, while physical therapy, compression bandaging, and hygiene manage swelling and prevent secondary infections.

Early diagnosis and intervention are crucial for preventing lymphatic filariasis progression to chronic stages. Elimination requires preventative measures and targeted treatment programs in endemic regions.

4.8. CLINICAL MANIFESTATIONS

4.8.1. ASYMPTOMATIC STAGE

In many cases, individuals infected with lymphatic filariasis may remain asymptomatic for years or even decades. During this stage, the parasites reside in the lymphatic vessels and nodes without causing noticeable symptoms. However, even in the absence of symptoms, the parasites



can still cause damage to the lymphatic system, leading to chronic inflammation and scarring (Paily et al. 2009).

4.8.2. ACUTE STAGE

Some people may experience acute episodes of inflammation known as acute adenolymphangitis (ADL). These episodes are characterized by sudden and painful swelling of the affected limb(s) (Fig. 4). ADL can be triggered by various factors, including secondary bacterial infections. The frequency of ADL episodes tends to increase over time (Dixit et al. 2007).

Lymphadenitis, Lymphangitis, and Lymphatic Filariasis are related conditions involving the lymphatic system. Let's explore each of them in detail:

4.9. LYMPHADENITIS

Lymphadenitis refers to the inflammation of the lymphatic system is filled with tiny, bean-shaped structures called lymph nodes. A vital role for lymph nodes in filtering lymph fluid, trapping harmful microorganisms and mounting an immune response to infections as shown in Fig. 5. (Mohapatra and Janmeja 2009).

4.9.1. CAUSES

Lymphadenitis is often caused by a bacterial or viral infection. Common pathogens include Staphylococcus aureus and Streptococcus pyogenes. The infection can occur when bacteria or viruses enter the body through wounds, bites, or other openings.(Colovic et al. 2008).

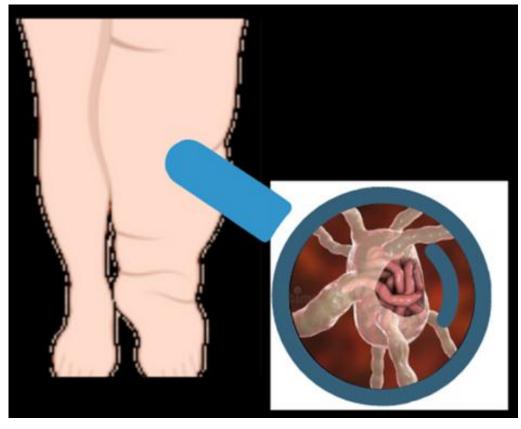


Fig. 4: Microscopic view of a person's leg with elephantiasis.3D view blockage of lymph node with filariasis worms.



4.9.2. SYMPTOMS

The affected lymph nodes become swollen, tender, and may feel warm to the touch. In some cases, the overlying skin might appear red or inflamed. Depending on the severity of the infection, one may experience fever, chills, and general malaise.

4.9.3. TREATMENT

Treatment typically involves antibiotics to address the underlying infection. Rest, pain relief medication, and warm compresses may also be recommended to alleviate symptoms (Weiler et al. 2000).

4.10. LYMPHANGITIS

Lymphangitis refers to the inflammation of the lymphatic vessels that transport lymph fluid from tissues to lymph nodes. It often develops as a complication of a skin infection, most commonly caused by Streptococcus or Staphylococcus bacteria.(Bruce et al. 1996).

4.10.1. CAUSES

The condition usually arises when bacteria enter the body through a wound or skin infection, spreading through the lymphatic vessels to the nearby lymph nodes.

4.10.2. SYMPTOMS

Lymphangitis is characterized by red streaks extending from the site of the wound or infection towards the nearest lymph nodes. The affected area may be swollen, warm, and painful. Other symptoms such as fever and chills may also be present (Klimek 2019).

4.10.3. TREATMENT

Antibiotics are the primary treatment for lymphangitis. Elevating the affected limb, rest, and warm compresses can help alleviate symptoms and promote recovery (Olszewski 2019).

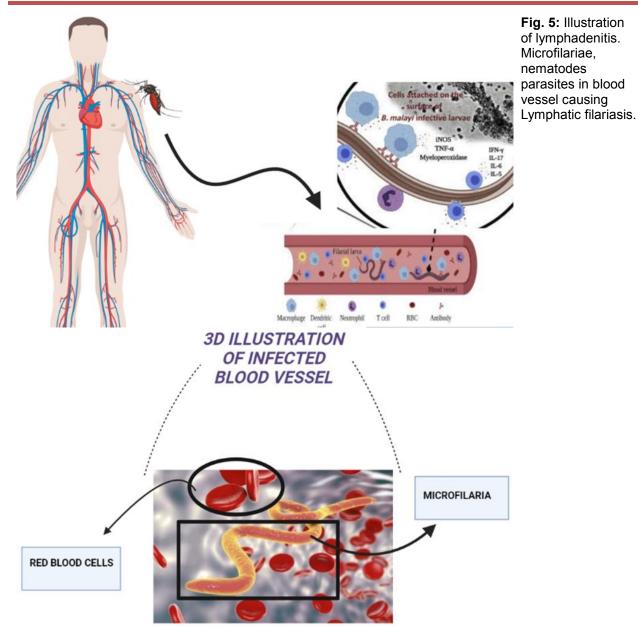
4.10.4. CHRONIC STAGE

Over time, repeated episodes of ADL and ongoing inflammation lead to chronic lymphatic obstruction. This condition is the hallmark of lymphatic filariasis and is responsible for the most visible and disabling symptoms associated with the disease.

4.10.5. LYMPHEDEMA

Chronic lymphatic obstruction causes a progressive buildup of fluid (lymph) in the affected limbs, leading to lymphedema. Lymphedema primarily affects the legs but can also occur in the arms, breasts, and genitals (Warren et al. 2007). The affected limb becomes swollen, heavy, and may exhibit skin changes, such as thickening and hardening (fibrosis). This chronic swelling can lead to permanent disability and disfigurement, resulting in the classic "elephantiasis" appearance as mentioned in Fig. 4 and 6. (Rockson 2001).





4.10.6. ELEPHANTIASIS

In severe cases of chronic lymphedema, the affected body parts can become grossly enlarged and thickened, giving rise to the term "elephantiasis." This condition most commonly affects the legs and genitalia and can result in significant physical and psychological distress for the affected individuals (Sisto and Khachemoune 2008).

4.10.7. HYDROCELE

In males, lymphatic filariasis can lead to the accumulation of fluid around the testicles, causing swelling known as hydrocele. The hydrocele can become quite large and cause discomfort (Dandapat et al. 1990).



4.10.8. UNDERSTANDING TROPICAL PULMONARY EOSINOPHILIA: CAUSES, SYMPTOMS, AND TREATMENT

Tropical pulmonary eosinophilia (TPE) is a condition caused by the immune response to microfilariae as shown in Fig. 7, which are tiny worm larvae transmitted through the bites of infected mosquitoes in areas with endemic lymphatic filariasis (Mullerpattan et al. 2013). When these microfilariae migrate to the lungs, they trigger an exaggerated immune reaction, leading to the accumulation of eosinophils, a type of white blood cell, in the lung tissues. Immune response triggers cough, wheezing, shortness of breath, and night fevers (Ottesen and Nutman 1992). TPE is a distinct clinical manifestation of lymphatic filariasis, characterized by elevated blood eosinophil levels and specific antibodies. Timely diagnosis and treatment with antifilarial drugs, such as diethylcarbamazine, can effectively manage TPE, preventing further complications and helping to control the spread of lymphatic filariasis in affected regions (Vijayan 2007).

4.10.9. LYMPHATIC FILARIASIS OF THE BREAST

In some cases, the lymphatic system of the breast may be affected, leading to swelling and enlargement of the breast.

It's essential to note that the severity of lymphatic filariasis can vary widely between individuals. Some may experience mild symptoms or remain asymptomatic, while others may develop severe and debilitating manifestations (Thongpiya et al. 2021).

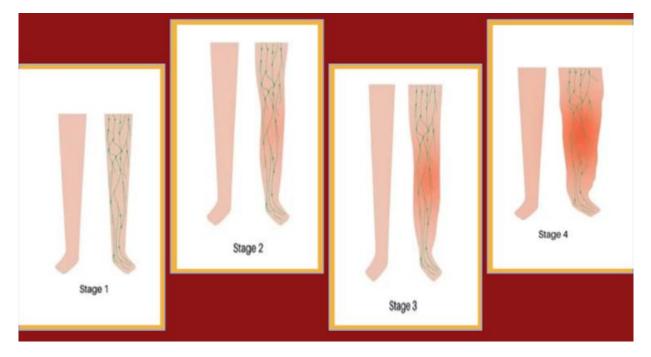


Fig. 6: Stages of Lymphedema Disease (Created by Biorender)

4.11. PREVENTION AND TREATMENT

Preventive measures primarily involve mosquito control, such as using insecticide-treated bed nets and mosquito repellents, and taking measures to reduce mosquito breeding sites (Dayal and Selvaraju 2010).



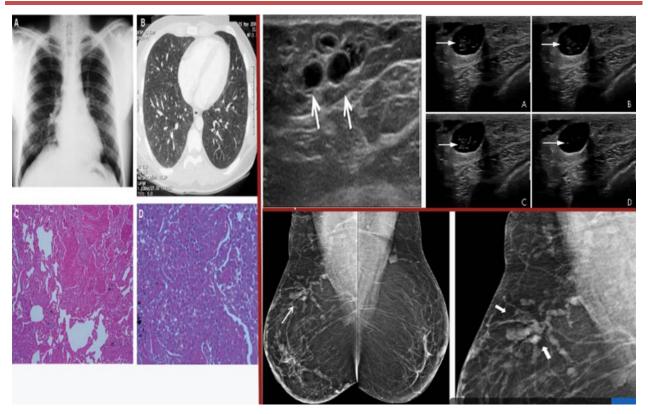


Fig. 7: Tropical pulmonary eosinophilia. Chest X-ray shows nodules, pattern of bilateral micronodule. Lung specimen with eosinophilic infiltration of alveolar sacs.

Mass drug administration with antifilarial drugs (such as diethylcarbamazine, ivermectin, and albendazole) is used to treat infected individuals and prevent the spread of the disease in endemic areas. For those already affected by the disease, managing and alleviating symptoms through good hygiene, elevation of affected limbs, compression bandaging, and exercises may help improve their quality of life. In severe cases, surgical intervention may be considered to reduce limb swelling and manage complications. Early diagnosis and timely intervention are crucial in preventing long-term disabilities associated with lymphatic filariasis (Chandy et al. 2011).

5. CONCLUSION

Parasite infections often persist despite attempts to completely eliminate them, as doing so might require harmful immune reactions from the host. Consequently, the manifestation of disease in many parasitic infections is often linked with immune-related damage. The most effective host response involves maintaining a balance in controlling the parasite within tolerable levels, thereby preserving immune equilibrium without causing permanent harm to tissues. Filarial infections exemplify the delicate interplay between hosts and parasites, where a harmonious immune-parasite equilibrium is occasionally disrupted, leading to severe consequences due to overwhelming host immune reactions.

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