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Overview of Filariasis

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Abstract
Lymphatic filariasis (LF) is a communicable tropical disease caused by filarial worms and transmitted through mosquito bites. The disease can lead to lymphedema, hydrocele, and permanent disability. This article presents an overview of the epidemiology, pathogenesis, diagnosis, management, and prevention of LF. The global program GPELF has contributed to a decline in cases through mass drug administration (MDA) and morbidity management. In Indonesia, the prevalence remains high, particularly in eastern regions. Early detection and comprehensive management are essential to support the sustainable elimination of filariasis.

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Introduction

Lymphatic filariasis (LF) is classified as a neglected tropical disease caused by infection with filarial worms such as *Brugia malayi*, *Brugia timori*, and *Wuchereria bancrofti*, with over 90% of global cases attributed to W. bancrofti. Transmission occurs via bites from mosquitoes of five genera: Anopheles, Mansonia, Culex, Aedes, and Armigeres. This infection can result in severe clinical complications such as lymphedema and hydrocele (Medeiros et al., 2021); (Chiphwanya et al., 2024).

In Indonesia, all three species are responsible for LF cases, with *Brugia malayi* accounting for approximately 70% of all reported infections (Rahmi, Sutiningsih, Hestiningsih, & Saraswati, 2022). Since 2000, the Global Programme to Eliminate Lymphatic Filariasis (GPELF) has committed to eliminating LF as a public health issue through two main strategies: (1) interrupting transmission via mass drug administration (MDA), and (2) managing morbidity and preventing disability in affected individuals (Titaley et al., 2022). The World Health Organization (WHO) launched GPELF in 2000 with the goal of eradicating LF globally by 2030. The program's strategy is based on stopping transmission through MDA and, at the same time, managing disease burden to alleviate suffering and prevent disability in those with chronic manifestations. MDA is designed to reduce infection levels the point where transmission is no longer sustainable.

For example, in areas where Aedes mosquitoes act as vectors, elimination is considered successful if the antigen prevalence (Ag) among children aged 6–7 years is below 1% (Lawford, Tukia, Takai, Sheridan, & Lau, 2024)

Epidemiology

An estimated 130 million cases of lymphatic filariasis (LF) have been recorded across 73 countries, with around 947 million people in 54 tropical and subtropical countries still at risk of infection. Approximately 15 million people suffer from lymphedema, while around 25 million men are affected by scrotal swelling due to hydrocele. This condition significantly reduces mobility, disrupts daily activities, and contributes to social isolation among those affected. In 1993, the International Task Force for Disease Eradication identified LF as one of six diseases considered potentially eradicable. In 1997, the World Health Assembly officially called for the elimination of LF as a public health problem, followed by the launch of the Global Programme to Eliminate Lymphatic Filariasis (GPELF) by WHO in 2000. According to WHO, approximately 120 million people across 81 tropical and subtropical countries have been infected, with one billion individuals at risk. An estimated 40 million people live with permanent disabilities, and in 2020, 863 million people in 50 countries required preventive treatment to stop disease transmission. Globally, around 25 million men suffer from hydrocele, and over 15 million individuals have lymphedema. At least 36 million people continue to experience symptoms of the disease (Gonzales, Noland, Mariano, & Blount, 2021); (Sinha et al., 2023)

In Indonesia, LF cases have been reported in nearly all provinces, with *Brugia malayi* accounting for around 70% of cases. In 2017, Papua had the highest number of endemic districts/cities, followed by East Nusa Tenggara, and Aceh, Southeast Sulawesi, and West Papua (12 each). According to 2018 data, 10,681 cases were reported nationally, with 236 of 514 districts categorized as endemic. In 2020, there were 9,906 recorded cases across all 34 provinces. Eastern Indonesia reported the highest numbers, with Papua recording 3,615 cases and East Nusa Tenggara 1,534. In Java, West Java recorded the highest number at 641 cases. Provinces like Bali, Yogyakarta, North Kalimantan, and

Gorontalo reported fewer than five cases each (Rahmi et al., 2022); (Kermelita, Hadi, Soviana, & Tiuria, 2023)

Pathogenesis

In the life cycle of lymphatic filariasis, an infected mosquito transmits third-stage larvae into the human host during a blood meal. These larvae penetrate the skin through the bite site and migrate into the lymphatic system, where they mature into adult worms. Female worms typically measure 80–100 mm in length, while males are around 40 mm. The females produce microfilariae—small, sheathed larvae measuring 244–296 μm in length and 7.5–10 μm in width—which exhibit nocturnal periodicity (Rajamanickam & Babu, 2025)

The microfilariae circulate through the lymphatic and blood systems and are taken up by mosquitoes during subsequent bites. Inside the mosquito, microfilariae shed their sheaths and migrate to the thoracic muscles, developing successively into first-stage, second-stage, and finally infective third-stage larvae. These larvae then travel to the mosquito's proboscis, making them ready for transmission during the next blood meal (Rajamanickam & Babu, 2025)

In humans, male and female worms mate, and a fertilized female can release up to 50,000 microfilariae into the bloodstream each day. Microfilariae can survive for several months, with a life span ranging from 60 to 100 weeks. Within mosquitoes, microfilariae take around 10–14 days to develop into infective larvae under optimal environmental conditions. Adult worms can live in the human body for 5 to 8 years, and in some cases, over 15 years (Rajamanickam & Babu, 2025)

The presence of adult filarial worms in the lymphatic vessels is the primary cause of pathological changes in LF. In endemic areas, a variety of clinical symptoms are observed, prompting extensive investigation into the disease's pathogenesis. Several studies have explored the connection between immune response and infection characteristics. Some individuals who are asymptomatic carriers with microfilaremia show suppressed immune responses to vaccines and co-infections. Based on current research, LF pathogenesis is generally categorized into two main pathways:(Widiastara, 2024)

The first pathway involves lymphangiectasia, or dilation of the lymphatic vessels, which is considered the initial lesion that occurs before the appearance of clinical symptoms. This dilation can affect individuals with adult filarial worms regardless of whether they show symptoms or have microfilaremia (Widiastara, 2024)

Adult filarial worms may induce lymphatic dilation and stimulate endothelial cell proliferation without completely obstructing the lymphatic system. This dilation can be influenced by host-derived proteins such as vascular endothelial growth factor (VEGF), angiopoietin, and matrix metalloproteinases. Additionally, antigens released by the worms themselves can stimulate endothelial growth and inflammation. These inflammatory responses are further exacerbated by the presence of Wolbachia—a symbiotic bacterium commonly found in Wuchereria - bancrofti and *Brugia malayi*—which plays a key role in the clinical pathogenesis of filariasis (Widiastara, 2024)

Lymphangiectasia and endothelial proliferation lead to acute dermatolymphangioadenitis (ADLA), characterized by swelling or edema in the affected limbs. Recurrent ADLA episodes can lead to chronic lymphedema. Skin damage resulting from swelling increases the risk of recurring secondary bacterial or fungal infections, which

significantly contribute to the development of filarial lymphedema and elephantiasis (Widiastara, 2024)

The second pathway focuses on clinical symptoms caused by the death of adult worms, either spontaneously or as a result of treatment. This triggers acute inflammation in local lymph nodes and lymphatic vessels, leading to acute filarial lymphangitis (AFL). Compared to ADLA, AFL episodes are usually less severe and rarely result in long-term lymphedema. [11]

AFL typically occurs in the intrascrotal lymphatic vessels, causing acute hydrocele due to temporary lymphatic obstruction from the tunica vaginalis. Most acute hydroceles resolve spontaneously within a short time. The exact risk factors for progression to chronic hydrocele remain unclear but may include direct effects of adult worms on the lymphatics, increased local hydrostatic pressure, granuloma formation, and rupture of dilated lymph vessels (Widiastara, 2024)

Clinical manifestation

Hydrocele is the most frequently observed clinical manifestation of lymphatic filariasis. In children, the infection often remains asymptomatic and usually becomes apparent after puberty, typically during the second or third decade of life (Newman & Juergens, 2023)

Other manifestations include:

Filarial fever – Presents with lymphangitis and lymphadenitis accompanied by nonspecific symptoms such as headache, fever, chills, and general malaise.

Filarial abscess – May form and result in localized swelling and pain; in some cases, the abscess ruptures and releases dead adult worms. Granulomatous reactions can cause nodules in subcutaneous tissue.

Acute Dermatolymphangioadenitis (ADLA) – Recurring episodes of lymphangitis that lead to the development of lymphedema.

Lymphedema – Classified based on severity ; *Grade I*: Pitting edema, reversible. *Grade II*: Pitting or non-pitting edema, non-reversible. *Grade III*: Non-pitting edema with skin thickening, non-reversible. *Grade IV*: Advanced skin thickening and nodularity (elephantiasis)

Tropical pulmonary eosinophilia (TPE) – An immune response to filarial infection, causing restrictive lung disease, wheezing, shortness of breath, and marked eosinophilia.

Diagnosis

Advancements in diagnostic technology have significantly improved the accuracy and efficiency of lymphatic filariasis detection (Shaukat et al., 2023)

Antigen Detection: Immunochromatographic test (ICT) and Filaria Strip Test (FST) provide high sensitivity and specificity for detecting W. bancrofti antigens, with results available within 1 to 10 minutes. ELISA using Og4C3 monoclonal antibodies is also effective for detecting W. bancrofti, though less so for Brugia species, which require alternative tests such as Brugia-specific ELISA or IgG4-based assays. These tests are often used for population screening or in settings requiring rapid results, though they may not distinguish between past exposure and active infection (Shaukat et al., 2023)

Molecular Techniques: PCR-based xenomonitoring is highly sensitive for detecting filarial DNA in both mosquitoes and humans, suitable for W. bancrofti and Brugia species. LAMP (Loop-Mediated Isothermal Amplification) offers a more field-friendly diagnostic tool with high sensitivity and specificity, especially valuable in low-resource settings or when confirmatory testing is needed (Shaukat et al., 2023)

Immunologic Markers: Elevated serum IgG and IgE levels—particularly IgG4—can indicate active infection, especially in tropical pulmonary eosinophilia. These are best used alongside other diagnostic methods for a comprehensive evaluation (Shaukat et al., 2023)

Parasitological Examination: Peripheral blood smears remain useful for identifying microfilariae, particularly considering their nocturnal periodicity. This method is best suited for detecting active infections in resource-limited areas but is less effective for chronic, low-level, or early-stage infections (Shaukat et al., 2023)

Ultrasonography: High-frequency ultrasound can detect live adult W. bancrofti worms in the scrotal lymphatics of asymptomatic men, although it is less effective for B. malayi. Peripheral blood smears are also valuable for chronic cases involving hydrocele or lymphedema

Lymphoscintigraphy: A diagnostic imaging technique used to assess lymphatic damage and dermal backflow in both symptomatic and asymptomatic cases. It helps differentiate filarial lymphedema from swelling caused by cancer, infection, or trauma, thus supporting appropriate treatment planning. These diagnostic tools have revolutionized LF detection, enabling more precise and timely identification of infections (Shaukat et al., 2023)

Management

Diethylcarbamazine (DEC) has long been recognized as an effective monotherapy for lymphatic filariasis; however, it should be avoided in individuals co-infected with Loa loa or onchocerciasis due to the risk of exacerbating eye complications and the potential for causing encephalopathy. Currently, the World Health Organization (WHO) recommends a triple-drug regimen combining a single dose of ivermectin, albendazole, and DEC in regions where Loa loa is not endemic. This combination has demonstrated the ability to eliminate microfilariae in up to 96% of infected individuals, with sustained effectiveness for up to three years. Doxycycline is the preferred treatment in Loa loa-endemic areas. In addition to its antiparasitic effects, doxycycline can reduce inflammation and fibrosis, which are key contributors to the progression of lymphedema. It also targets the Wolbachia bacterium, an endosymbiotic organism found in filarial worms, which has been a major therapeutic target for more than a decade. This has led to various field trials evaluating the effectiveness of several antibiotic classes, including tetracyclines (e.g., minocycline, doxycycline), rifamycins (e.g., rifampicin, rifapentine), azithromycin, and chloramphenicol (Newman & Juergens, 2023); (Annashr & Rahmadi, 2021)

Currently, there is no available vaccine for filariasis, but ongoing research aims to develop one in the future (Newman & Juergens, 2023)

In addition to pharmacological treatments, surgical interventions can be employed to reduce tissue buildup and improve lymphatic drainage through lymphovenous anastomosis procedures. Topical coumarin and flavonoids have been shown to be effective in alleviating lymphedema, likely by enhancing macrophage activity, which facilitates the resorption of protein-rich fluids from affected tissues (Newman & Juergens, 2023)

A case report documented the success of ablative carbon dioxide laser therapy in treating skin lesions and lymphocutaneous fistulas, resulting in significant improvement. This treatment works by inducing thermal damage in the dermis, promoting skin remodeling and dermal tightening. Although initially used for non-filarial elephantiasis,

the method shows potential for application in filarial disease cases as well. Lymphedema can also develop as a consequence of repeated episodes of adenolymphangitis, even in the absence of LF infection. Strategies to prevent the progression of lymphedema include patient education on proper skin hygiene, wearing comfortable

footwear, applying compression bandages, utilizing pneumatic compression devices, regularly washing with soap and water, elevating limbs, applying hot/cold therapy, and using topical antibiotics or antifungal creams to prevent recurrent lymphangitis (Newman & Juergens, 2023)

Prevention

The Mass Drug Administration (MDA) program for filariasis is a government-led initiative implemented in districts and cities classified as endemic areas. This treatment is carried out once a year and is administered to the entire population in the target area. The objective is to simultaneously eliminate microfilariae from the blood circulation of all residents to interrupt transmission. This initiative, coordinated globally by the Global Programme to Eliminate Lymphatic Filariasis (GPELF), has significantly reduced the prevalence and burden of filariasis around the world. By decreasing the density of circulating parasites in infected individuals, the program helps to lower community-wide infection rates, thereby minimizing the risk of continued transmission through mosquito vectors (Annashr & Rahmadi, 2021)

Prognosis

The prognosis for lymphatic filariasis is generally favorable if the disease is detected early and treated appropriately to prevent disfigurement. The infection typically responds well to five annual doses of DEC, either alone or in combination with ivermectin or albendazole. Symptoms often do not appear until adulthood and tend to correlate with the increasing burden of adult worms in the body. The most severe form of the disease is elephantiasis, which results from long-term acute and chronic infections. Although several treatment options exist for managing lymphedema, it becomes increasingly difficult to treat once the disease has reached an advanced stage (Newman & Juergens, 2023)

Complications

Untreated lymphatic filariasis can lead to a range of complications, including tropical pulmonary eosinophilia, filarial arthritis, severe glomerulonephritis associated with filariasis, filarial mastitis, and loiasis, which is a parasitic infection frequently linked to filariasis (Newman & Juergens, 2023); (Cindy & Ivonne, 2023)

Conclusion

Lymphatic filariasis (LF) is a neglected tropical disease caused by filarial worms, with *Wuchereria bancrofti* being the primary agent worldwide, including in Indonesia. The disease is transmitted through mosquito bites from various genera, such as Anopheles, Mansonia, Culex, Aedes, and Armigeres, and can result in serious clinical conditions such as lymphedema and hydrocele.

The Global Programme to Eliminate Lymphatic Filariasis (GPELF), launched in 2000, aims to eliminate LF through two core strategies: interrupting transmission via mass drug administration (MDA) and managing morbidity to prevent long-term

disability. Routine MDA programs have proven effective in reducing both the prevalence and morbidity of LF globally.

If detected and treated early, the prognosis is good. However, if left untreated, the disease may progress to elephantiasis, the most severe and challenging stage to manage.

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