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A Rare Disease on the Rise: Mysterious Swelling in ER Patient Leads to Massive Outbreaks in Southern Ontario

*The case presented is based on a real-life report published in 2024 regarding a patient with a 10-year history of stage 4 lymphedema[1]

A 72-year-old man presented at the ER yesterday morning with edema (swelling) of the left lower limb, difficulty walking, and fever. The affected limb was enlarged, non-pitting (indentation did not persist after pressure), hardened, and hyperpigmented, with cobblestone-like lesions (Figure 1). Additionally, the surrounding tissue was warm to the touch and tender. Upon further examination, doctors noted an elevated white blood cell count (16,000/uL). Following diagnostic testing, the patient was determined to be in the advanced stage of elephantiasis and was eventually treated using chemotherapy with Diethylcarbamazine (DEC).

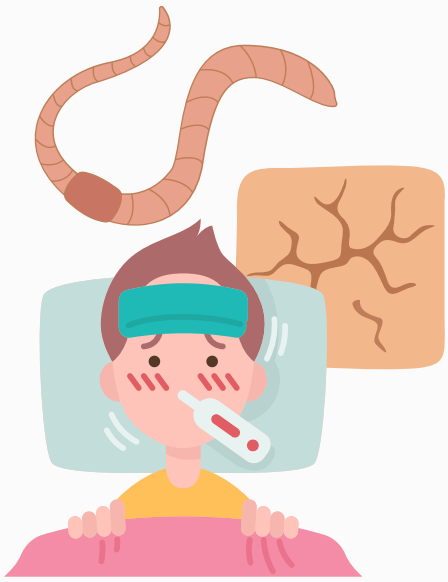
While once considered rare in Canada, cases like this are becoming increasingly common. In recent years, accelerating climate change has driven the northward migration of mosquito vectors carrying elephantiasis from developing equatorial nations.

Figure 1. Edematous left lower limb. Adapted from Ledwani and Karnan.[1]

As temperatures continue to rise, hospitals are reporting growing numbers of infections, with emerging hotspots in London, Ottawa, and the Greater Toronto Area. Epidemiologist John Smith warns that this trend is likely to continue and recommends preventative measures such as wearing long sleeves, using insect repellent, and limiting outdoor activity during dawn and dusk.

Elephantiasis

Elephantiasis, also known as lymphatic filariasis, is an infectious disease caused by parasitic worms and transmitted by mosquito bites[2]. This disease is characterized by thickening of the skin and muscles on limbs, genitalia, and breasts[2]. There are two types of elephantiasis: lymphatic filariasis and non-filarial elephantiasis. Lymphatic filariasis is caused by parasitic worms, while non-filarial elephantiasis can be caused by illnesses such as tuberculosis, leprosy, leishmaniasis, recurrent streptococcal infections and STIs.[2] It can also be caused by long-term exposure to irritant soils[3].

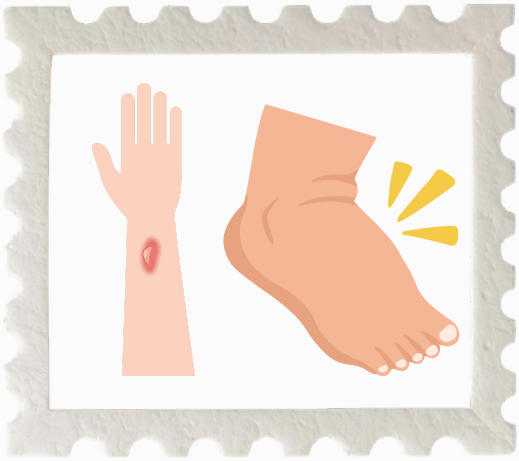


Symptoms of Elephantiasis

Symptoms of elephantiasis vary in severity depending on the stage of the disease. In earlier stages, individuals are either asymptomatic or experience mild symptoms such as a cold, chills, and fevers[4]. When the disease becomes chronic, individuals experience symptoms such as lymphedema (swelling of tissues), thickening of the skin and tissues, and hydrocele (swelling of the scrotum)[5]. Elephantiasis can also cause local inflammation on the skin, lymph nodes and lymphatic vessels[5].

Edema

Edema is the medical term for swelling that is caused by excess fluid building up in the body's tissues[6]. Edema has two forms: localized and generalized. Localized edema occurs in a smaller area on one specific part of the body. This form of edema is considered relatively safe as it is a natural part of the body's healing process[6]. In comparison, generalized edema affects a larger area of the body or is systemic, making it more serious[6]. Edema commonly occurs on the feet, ankles, legs, hands, face, and stomach. It can impact individuals of any age; however, adults over the age of 65 are more prone to this condition[7]. Pregnant women, individuals with blood clots and individuals on medications such as calcium channel blockers, NSAIDs, steroids, estrogens and some diabetes medications may also face a higher risk for getting edema[7].



Symptoms of Edema

Some of the common symptoms of edema include swelling in the ankles, feet, hands, face, and arms, coughing or trouble breathing, pain in the affected area, difficulty walking or moving certain joints, weight gain due to extra fluids and skin that appears shiny or stretched[7].

Demographics: Is it more prevalent/severe in certain individuals?

Elephantiasis is a widespread global health issue that impacts approximately 120 million people across the world in Asia, Africa, South America, the West Pacific, and parts of the Caribbean[2]. This makes it the **second most** prevalent vector-borne disease, following malaria[2]. Although elephantiasis has a relatively low mortality rate, it can often lead to permanent disability. Individuals affected often also struggle with their social, mental, and financial well-being[5]. Elephantiasis can affect individuals at any age; however, adults who develop this disease in their 30s and 40s are more prone to developing severe complications[8] .

TRUE OR FALSE?

1. Elephantiasis is the second most prevalent vector-borne disease following malaria

2. Edema is asymptomatic in its early stages

POP QUIZ

What are the symptoms of elephantiasis?

a. coughing or trouble breathing

b. lymphedema, hydrocele, and thickening of the skin and tissues

c. swelling in parts of the body

Answer Key:
True or False:
Q1. T
Q2. F
Pop Quiz: b

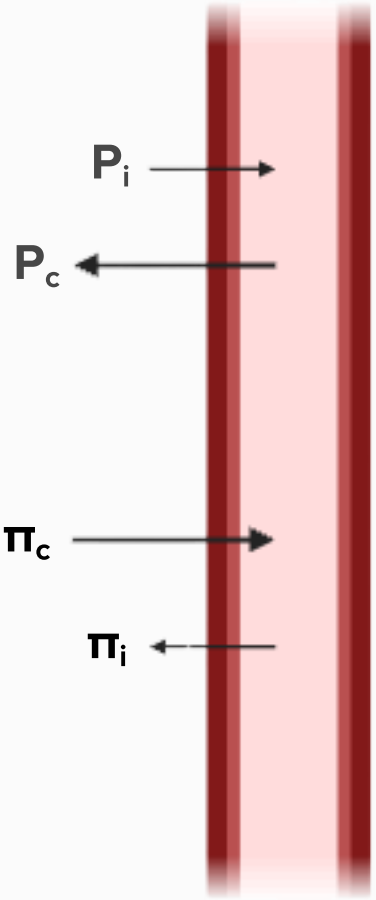
Starling Forces: Principles of Fluid Filtration

WHAT DRIVES FLUID TO LEAK OUT OF CAPILLARIES INTO THE INTERSTITIAL SPACE?

This process is governed by the Starling Principle, first proposed by Ernest Starling in 1896 when he observed that the presence of a hemorrhage causes blood to become more dilute.[9] He proposed that fluid must be moving between the blood vessels and surrounding tissues. Through subsequent refinement, the modern Starling equation was developed[9,10]:

$$J_v = K_f[(P_c - P_i) - \sigma(\pi_c - \pi_i)]$$

Where,
Jv = net fluid movement
Kf = filtration coefficient (membrane permeability × surface area)
Pc = capillary hydrostatic pressure
Pi = interstitial hydrostatic pressure
σ = reflection coefficient (protein permeability factor)
Πc = capillary oncotic pressure
Πi = interstitial oncotic pressure



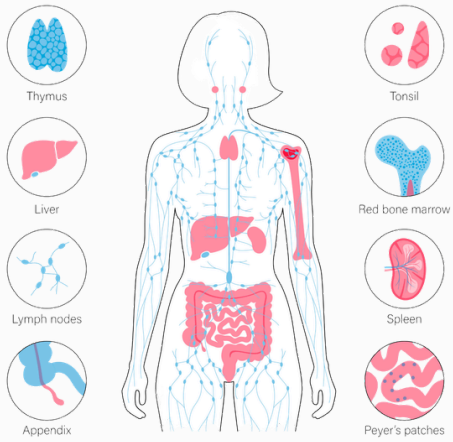
Made with BioRender

Hydrostatic pressure refers to the force exerted by fluid against the capillary wall, originating from blood pressure within capillaries (Pc) or interstitial fluid outside them (Pi).[10] In contrast, oncotic pressure is generated by large proteins that cannot cross the capillary wall. Plasma proteins create capillary oncotic pressure, increasing the osmolality of blood to draw fluid into capillaries.

Meanwhile, proteins in the interstitial space generate interstitial oncotic pressure, pulling fluid outward. The magnitude and direction of fluid movement depend on the balance between these opposing forces. At the arteriolar end of a capillary, the capillary hydrostatic pressure is high and exceeds opposing forces, driving net filtration of fluid into the interstitial space.[9,10]

As blood moves toward the venous end, capillary hydrostatic pressure decreases, allowing capillary oncotic pressure to dominate and draw some fluid back into the blood. However, filtration overall exceeds reabsorption. The excess fluid that remains in the interstitial space is collected by the lymphatic system. This continuous drainage is essential for preventing edema and maintaining tissue homeostasis.[10]

The Lymphatic System

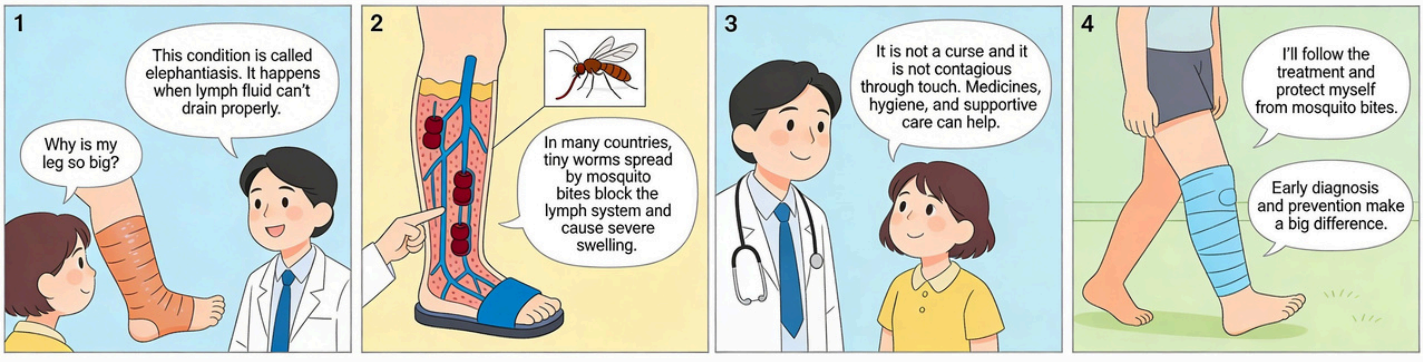


The lymphatic system is a network of organs, vessels, and tissues that are responsible for returning excess interstitial fluid (lymph) to the bloodstream.[11] It extends throughout most of the body, including the brain and eyes.[12,13] In addition to maintaining fluid balance, the lymphatic system plays an important role in immunity and the absorption of dietary fats, large proteins, and some vitamins.[14]

Lymphatic Drainage

Every day, around 20 liters of plasma leak out of vascular capillaries to deliver oxygen and nutrients to the surrounding tissues.[11] While most of this liquid is reabsorbed, the remainder must be cleared to prevent accumulation in the interstitial space. Lymphatic drainage begins with lymphatic capillaries, which take up excess fluid, cell debris, and macromolecules.[11, 14] These capillaries converge into progressively larger collecting vessels, which possess abundant smooth muscle and one-way valves to facilitate pumping and prevent backflow.[11] .

Anchoring filaments tether the vessel endothelium to surrounding connective tissue, preventing collapse during pressure changes. As lymph travels through the lymphatic vessels, it passes through numerous kidney-shaped lymph nodes.[11, 14] These structures act as filters to eliminate pathogens and foreign particles while housing large populations of lymphocytes embedded within a reticular network.[11] Each lymph node is enclosed within a fibrous capsule that dips deeper into the tissue in the form of trabeculae, providing structural support. Following filtration, lymph is transported to the thoracic duct or the right lymphatic duct and returned to the blood via the subclavian veins.



Lymphatic Pumping Mechanics

Because lymph must be transported centrally against hydrostatic pressure and protein concentration gradients, the lymphatic system relies on active pumping.[13] This is achieved through rhythmic contractions of lymphatic muscle cells that are synchronized over the length of a lymphangion, the elementary pumping unit of a lymphatic collecting vessel located between consecutive intraluminal valves (Figure 2). These contractions arise from intrinsic pacemaker activity in lymphatic smooth muscle and associated interstitial cells. Electrical signals are generated through ion channels, including fast Na+ channels and T-Type Ca2+ channels, and are propagated to neighbouring cells through gap junctions.[12]

This activity triggers Ca2+ influx through L-type, voltage-gated channels, as well as the resultant release of Ca2+ from intracellular stores.[12] The increase in cytoplasmic Ca2+ enables binding to calmodulin, activating myosin light chain kinase (MLCK), which phosphorylates myosin to initiate muscle contraction. Conversely, myosin light chain phosphatase (MLCP) dephosphorylates myosin, promoting relaxation. As such, the balance between MLCK and MLCP activity regulates lymphatic muscle contraction.[13]

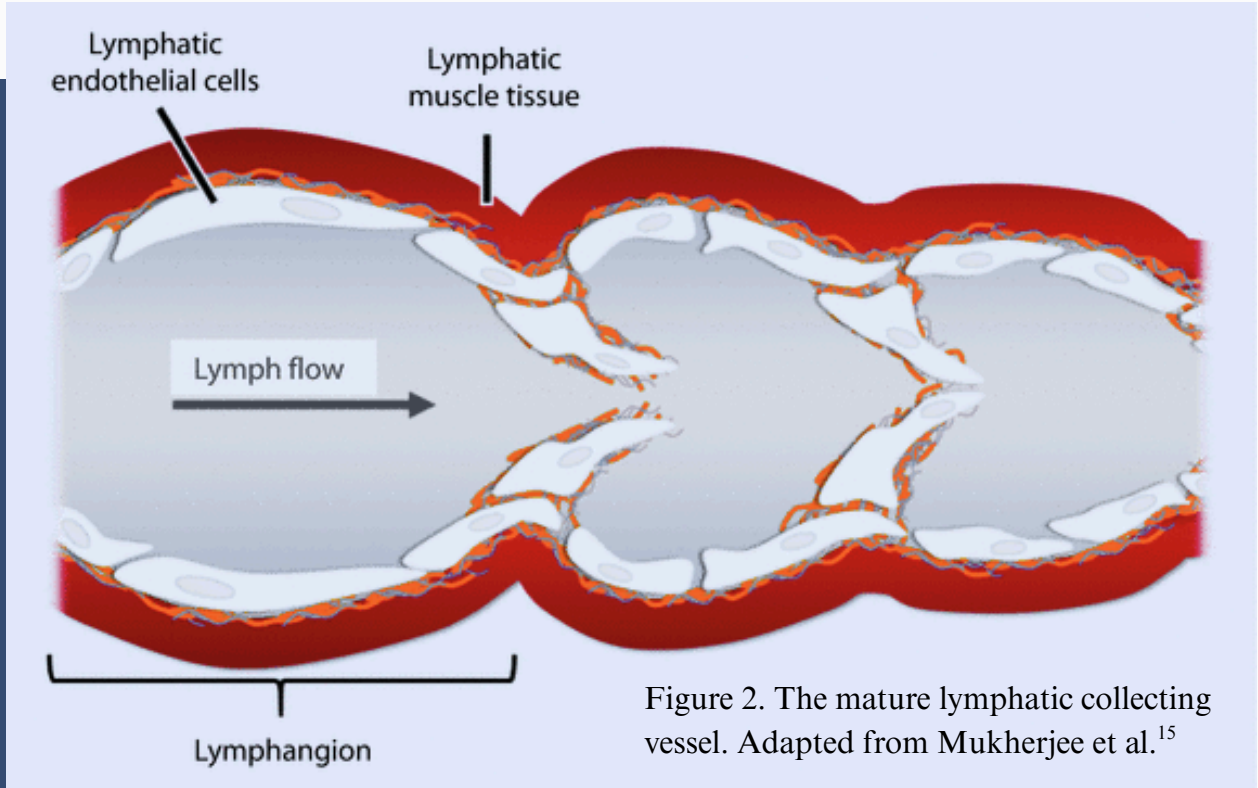


Figure 2. The mature lymphatic collecting vessel. Adapted from Mukherjee et al.[15]

Etiology

Elephantiasis is a condition that can develop due to filariasis, a parasitic infection transmitted through mosquito bites. Several types of filarial worms cause filariasis. *Wuchereria bancrofti* accounts for 90% of cases globally, while *Brugia malayi* and *Brugia timori* cause the remaining 10% of infections.[16] In many cases, people are infected with the disease in childhood, but are asymptomatic until later in life.[17] Not only that, but it usually takes many mosquito bites over a long period of time in a susceptible area for an individual to become infected.[18]

Specific mosquito genera, such as *Aedes, Anopheles, Culex,* or *Mansonia*, are necessary for larval development of the parasite and transmission to human hosts.[16] When the mosquito vectors feed on human blood, they ingest microfilariae, allowing the larvae to grow and become infective. These infective larvae are deposited and breach the skin barrier when the mosquito feeds. Once deposited, the larvae migrate to the host's lymphatic system, where they undergo two more moults to develop into adult worms.[16]

These adult worms then live in lymph nodes, in the afferent lymphatics, or sinuses. The lifespan of adult worms is about 5-7 years, but the damage persists even after the worms die.[17] The female worms release thousands of microfilariae into the host's lymphatic circulation, which migrate from the lymph into the peripheral circulation. Mediators released by the adult worms cause vessel dilation, which gradually impairs lymphatic contractility. As the damage progresses, "stasis of lymph tends to occur in the dilated vessels due to incompetence of the unidirectional valves," as stated by a study on lymphatic filariasis.[16]

Consequent dermato-lymphangio-adenitis can occur due to bacterial or secondary infections that further damage the lymph nodes. Frequent instances of lymphangio-adenitis can cause lymphedema, which can progress into elephantiasis and hydrocele.[16]

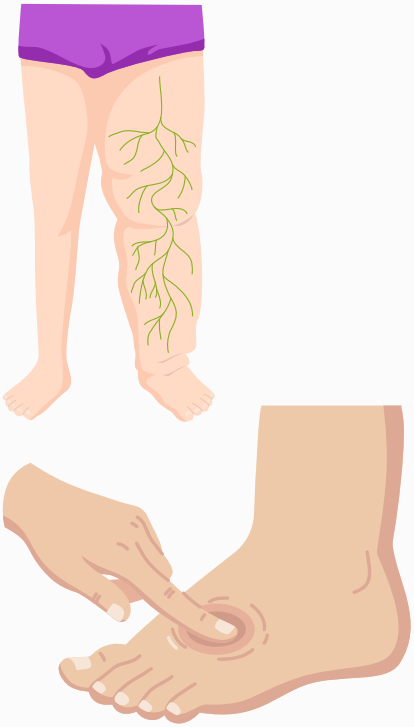
Four factors are critical in the onset and progression of lymphatic filariasis: the living worm, the inflammatory responses caused by the adult worm's death, secondary bacterial infections, and microfilariae.[16] Acute or asymptomatic manifestations of lymphatic filariasis occur due to microfilariae and adult worms.[16] From there, the diseased state progresses into a chronic condition due to dead and decalcifying worms.[16] Following this, lymphedema occurs, and if it is not resolved in its early stages, it can progress to elephantiasis, which is an irreversible pathological state. Both lymphedema and elephantiasis result from impaired lymphatic drainage, often caused by the obstruction of lymphatic vessels by adult worms nests and secondary infections.

Lymphedema Staging

According to Greene and Goss,[19] there are two stages of lymphedema. Primary lymphedema is idiopathic and caused by an "error in lymphatic development," while secondary lymphedema is acquired and is a direct consequence of an injury to a normal, developed lymphatic system.[19] Lymphatic filariasis, otherwise known as elephantiasis, is caused by secondary lymphedema.

Progression is the same for both primary and secondary lymphedema:

Stage 0 lymphedema: no visible swelling, and the extremities look relatively unaffected, but lymph transport is affected.[19]
Stage 1 lymphedema: early edema that can be resolved by elevating the limb.[19]
Stage 2 lymphedema: pitting edema that cannot be improved with limb elevation.[19]
Stage 3 lymphedema: fibroadipose deposition and subsequent changes to the skin as the affected area increases in size due to accumulated interstitial lymphatic fluid that causes subcutaneous fibroadipose production.[19]



Non-filarial elephantiasis: How does it occur?

Non-filarial elephantiasis, also known as podoconiosis, is a condition driven by genetic and environmental factors, with no infectious biological agents identified as a cause. For instance, exaggerated T-cell mediated inflammatory responses in the lymph nodes have been associated with podoconiosis.[3] In terms of environment, podoconiosis is frequently attributed to irritating soil particles found in red clay soils, such as volcanic soils.[2] Smectite clays or certain elements such as zirconium, aluminium, and beryllium may also contribute to non-filarial elephantiasis.[3] It can also be caused by illnesses such as tuberculosis, leprosy, leishmaniasis, recurrent streptococcal infections, and sexually transmitted diseases like lymphogranuloma venereum.[2]

What are the traditional treatments for elephantiasis?

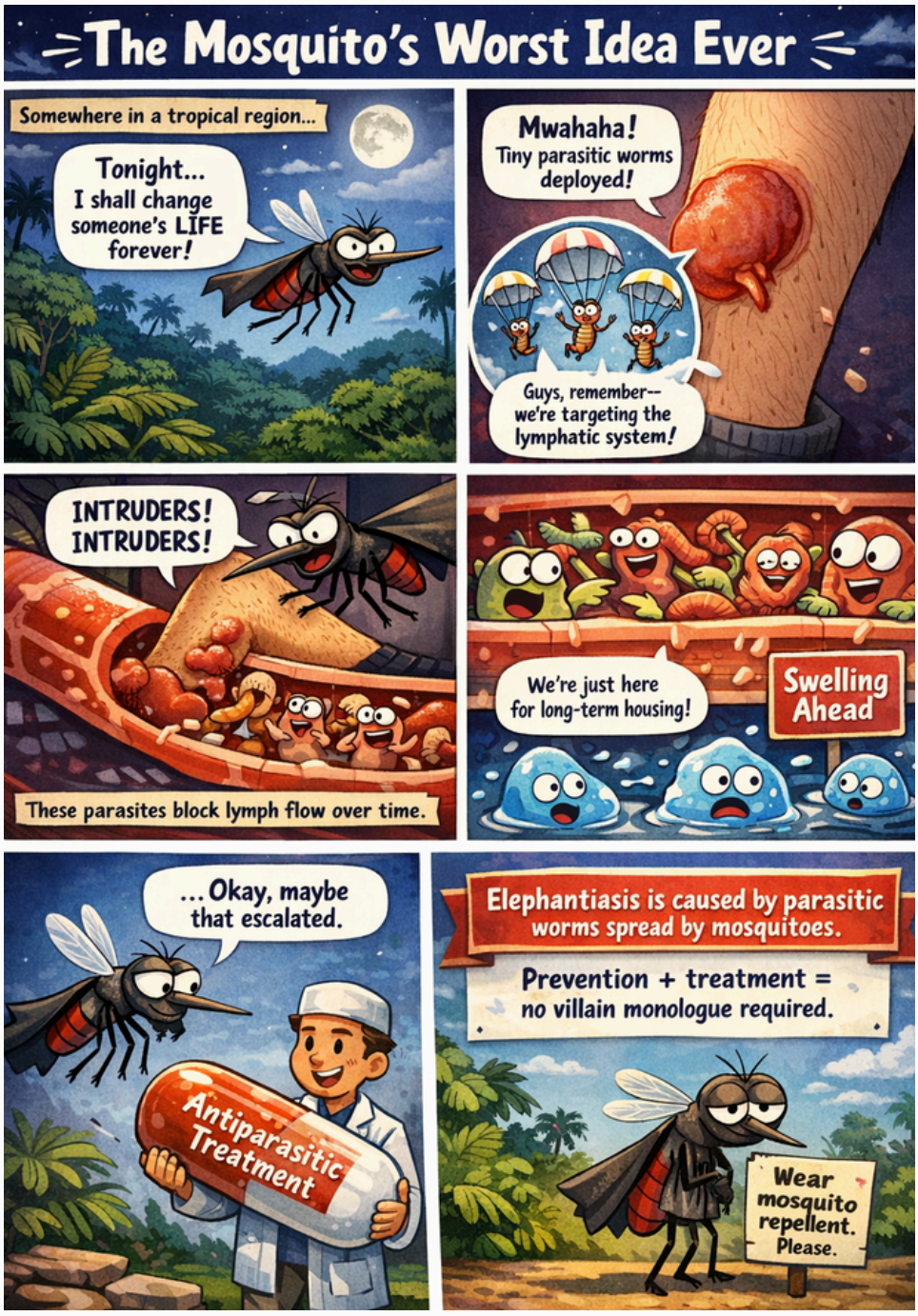
Current treatment of lymphatic filariasis focuses on antiparasitic medications that target the underlying infection and limit transmission. Common drugs include Ivermectin (Stromectol®), Diethylcarbamazine (Hetrazan®), and Albendazole (Albenza®), which work by destroying adult worms in the bloodstream or preventing their reproduction.[18] These treatments also help reduce the spread of infection to others. In addition, surgery may be required to remove dead worms or to relieve complications such as a hydrocele, where fluid accumulates in the scrotum.[18] Management of swelling is also important, with healthcare providers recommending supportive strategies such as limb elevation and compression garments.[18] On a broader scale, global prevention relies on mass drug administration (MDA); the World Health Organization recommends specific drug combinations depending on regional co-infections, including regimens using albendazole alone, ivermectin with albendazole, diethylcarbamazine with albendazole, or a triple-drug combination.[5]

What are the novel therapies for elephantiasis?

Recent advances in treatment have focused on restoring lymphatic function and improving quality of life. Intensive decongestive therapy has shown promising results, reducing limb volume by approximately 50% within one week and achieving near-normalization over several weeks, depending on disease severity.[20] The Godoy & Godoy method is a newer approach that combines manual lymphatic therapy, cervical stimulation, mechanical lymphatic therapy, and compression techniques to normalize or nearly normalize lymphedema, even in advanced elephantiasis.[20] Surgical innovations such as lymphatic system transplantation, vascularized lymph node transfer, and liposuction aim to restore lymphatic circulation and reduce swelling.[23] Additionally, early physiotherapy interventions play a key role in improving functional recovery and enhancing long-term outcomes for patients.[21]

What happens if elephantiasis is not treated?

If left untreated, elephantiasis leads to chronic lymphatic obstruction and persistent edema, resulting in irreversible tissue changes.[22] Over time, affected limbs or body parts become massively enlarged, with significant skin thickening and fibrosis.[22] This progression not only causes severe physical disability but also increases susceptibility to recurrent cellulitis, a bacterial skin infection that can further worsen the condition.[22] The disease can become profoundly debilitating, as reflected in patient experiences describing intense pain and life-altering impacts.



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WORD BANK

elephantiasis
edema
mosquito
lymph
ivermectin
albendazole
microfilariae
swelling
cough
inflammation
draining
parasitic
lymphangion
contraction
podoconiosis

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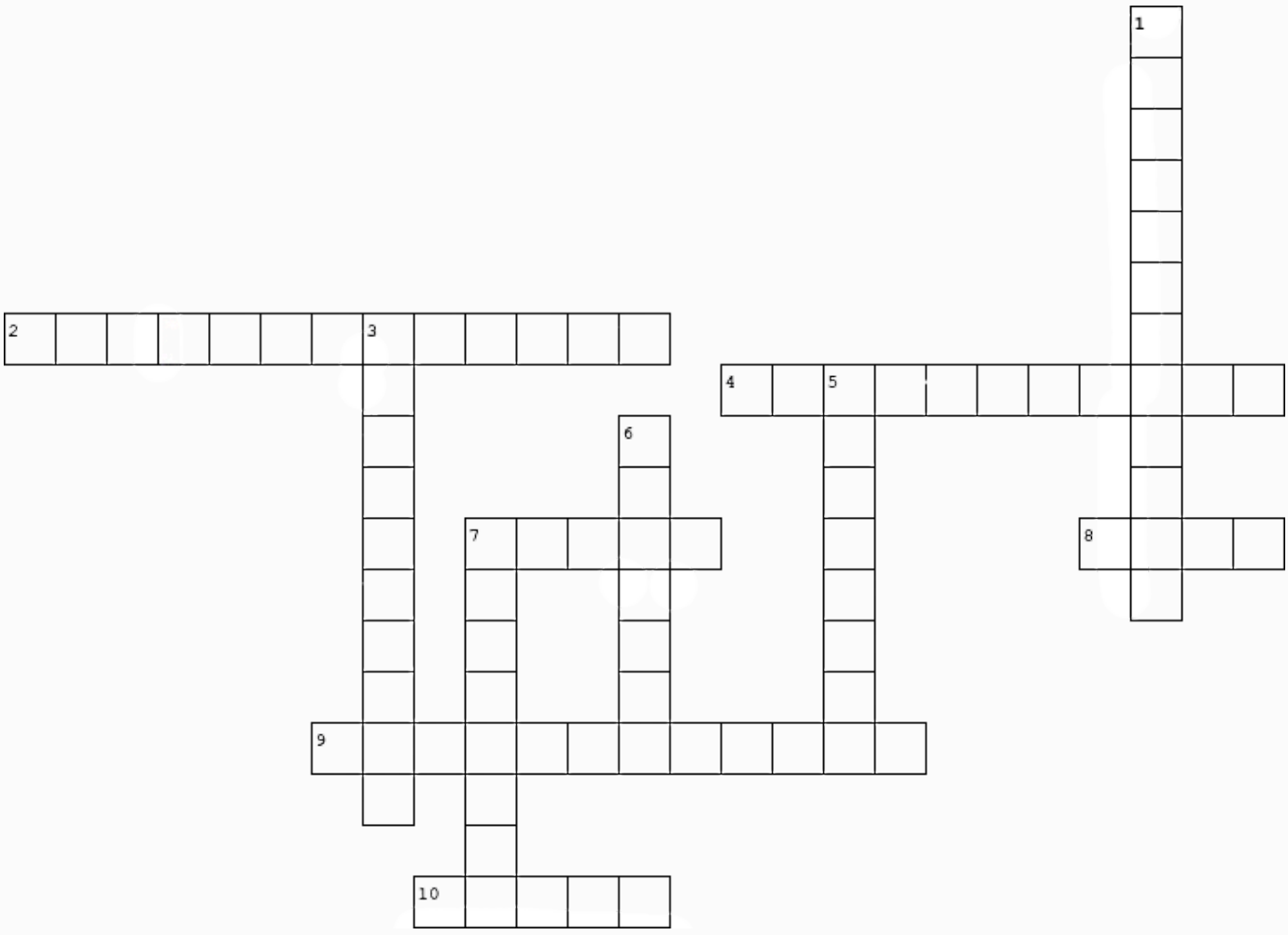

Across

2. A condition caused by an infection with parasites

4. The elementary pumping unit of a lymphatic vessel

7. Swelling caused by excess fluids trapped in the body's tissues

8. Objective evidence of disease

9. Immune response

10. Fluid in the immune system

Down

1. Non-filarial elephantiasis

3. Type of novel treatment

5. Insect vector for elephantiasis

6. Subjective evidence of disease

7. the cause of a disease or condition

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