Chapter

Understanding the Pathogenesis of the Major Human Filarial Nematode Infections

Charles D. Mackenzie, Wilfred L. Mandara and Esther Mwakitalu

Abstract

Filarial infections are very common across the animal kingdom despite their tendency to be host specific. Although often being silent infections with relatively little clinical consequence, three filarial infections can cause significant morbidity: onchocerciasis (OV) (caused by *Onchocerca volvulus*) and lymphatic filariasis (LF) (caused by *Wuchereria bancrofti* or *Brugia sp*), and in the veterinary world, the common canine condition of dirofilariasis. Successful elimination programs for these have been developed in the endemic countries based on extensive chemotherapy distribution, and these have catalysed a much greater understanding of the treatment and epidemiology of these infections. In contrast, the pathogenesis and clinical presentation of the two human filarial diseases, and a third, loiasis—which can complicate chemotherapy distribution in OV and LF co-endemic areas—are still not well understood. This present discussion addresses recent knowledge concerning the pathogenesis and presentation of the two major human filariases and makes suggestions as to approaches that could be taken to better understand their pathobiology and clinical forms. Better understanding and improved monitoring of the clinical condition are both likely to augment the already successful progress to global elimination.

Keywords: lymphatic filariasis, onchocerciasis, pathogenesis, investigation, assessment

1. Introduction

Nematode infections are complicated and still poorly understood infectious agents. The fact that being large, anatomically and biochemically complex organisms they can still live and multiply within their hosts (**Table 1**), often without any obvious clinical signs and symptoms, reflects a remarkable degree of adaptation they have undergone during their evolution. Filariae are arguably the most extraordinary of the nematode species, which are widely distributed throughout nature in being present in many host species, although are nevertheless often confined to a single host species. It should also be noted that non-filarial nematodes can also be present in their host without obvious external indications—a classical example being *Ascaris sp.* which migrates through the body, arguably through the circulation, without major clinical

Stage/component	Characteristic	Location	
L1	Microfilaria	Host and vector	Identifiable
L2	Intra-vector stage	Vector	Identifiable
L3	Infective stage	Vector and host	Identifiable in vector
L4	Relatively short-lived developing stage	Host- little known	Not identified
L5/Adult	Long lived		Identifiable
Uterine components	Biologically active in the host		Identifiable

Table 1.
Different stages in the development of a filarial nematode.

external signs to the lungs to finally reach the intestine again with a mild cough being the only obvious clinical presentation. However, filariae are parasites that do not just migrate through their host's internal tissues but also mate and multiply within the host's tissues, a biologically complex activity that arguably requires a high level of adaptation, or manipulation, of the host's natural ability to react to and reject foreign materials and substances. This present communication aims to describe recent changes in our understanding and perceptions of the major filarial diseases, and to emphasise that it is important, if there are to be useful advances in the global progress to elimination filarial infections, to better understanding their pathobiology and clinical presentation.

Historically filarial infections have generally been placed in the category of "clinical oddities" and have been commonly known by somewhat emotive titles: "River Blindness" for onchocerciasis, "Calabar Swelling" for loiasis, and "elephantiasis" with LF [1, 2]. All of these titles actually lack accuracy as appropriate descriptors of the actual infections. Onchocerciasis is more commonly a dermatological condition rather than an ophthalmic disease—although the blindness induced in severe cases is undoubtedly clinically significant. Loiasis is known more commonly now as "eye worm"—due to observable passage of the adult worm across the conjunctiva, which is more common than the sub-dermal swellings. Clinically, loiasis is better known for the adverse central nervous system responses that can occur post chemotherapeutic treatment rather than a serious clinical disease in its own right. Use of the term "elephantiasis" for LF is now regarded as being unacceptable in a disease that is associated with high levels of stigma in those affected—comparing this condition to an elephant's skin is not appropriate for either the human, or the innocently defamed elephant. Unfortunately, this condition is already extraordinarily well known across the globe by the term "elephantiasis," as is the image of the dramatic scrotal swelling that occurs due to hydrocoele induced by LF infection. Thus, it is important that we learn more about the characteristics of these diseases through careful observation and operational investigations and that we change old perceptions through dissemination of new data driven by new, well-investigated, information about their pathogenesis, interpretation, and treatment.

Our general understanding of filarial infections today has been largely driven by two major issues—firstly, the search for an effective and safe chemotherapeutic treatment and secondly, the decision that the major two of these groups' human filarial infections, onchocerciasis (*Onchocerca volvulus*) and the lymphatic filariae (*Wuchereria bancrofti* and *Brugia* sp.) could be controlled and subsequently eliminated [3]. The latter of the two by either through interrupting transmission as

with human onchocerciasis, or in the case of human LF by reducing infection and morbidity so that it is no longer a major public health problem [1]. The other filarial nematode that has featured historically in terms of research and clinical documentation is the canine infection *Dirofilaria immitis* (canine "heart worm"), which has been a major veterinary condition many years. Although experimental models do feature strongly in the history of investigation into filarial infections, these have often been largely directed towards the development of new anti-filarial drugs or immunological aspects rather than on increasing our understanding the pathogenesis and other areas of the pathobiology of these fascinating abundant animals.

The first of the common driving factors, the search for more effective chemotherapeutic regimes, has been catalysed by the fact that the drug effects on the parasites, especially those lying in sensitive tissues, such as those of the skin (where many inflammatory pathways can be activated), often is associated with severe and often life-threatening adverse reactions. Thus, there has been a need to develop safe chemotherapeutic regimes, especially as these treatments are now used in mass drug administration projects where millions of people in OV and LF endemic countries receive these drugs. Understanding these adverse reactions has itself catalysed filarial research and has led to better understanding of the pathogenesis of these infections. One example of this how the acute phases of oncho-dermatitis were clarified—observing the rapid clinical dermal reactions following the administration of the microfilaricidal agent diethylcarbamazine (DEC) enhanced our understanding of the natural responses in the skin when the microfilariae die and cause focal lesions. Likewise, the second of these major driving factors, the attempts to control and eliminate OV and LF, has required a better definition of their epidemiology, and more specifically their rapid detection. In addition, the global elimination programs have catalysed interest in these often ignored chronic diseases in the medical community of endemic countries.

It could be argued that all the interest and support given to endemic country-based elimination programs has ironically been counter-productive to gaining more knowledge on the more fundamental patho-biological aspects of these diseases; pathogenesis and clinical understanding becoming the poor cousins of the major two components, drug development and epidemiological elimination. This is not to say that the advances in these major two components have made has not been in many ways spectacular and a great credit to medicine and allied bodies; they indeed have been, and their major aims are being slowly achieved [3, 4]. There are, however, important facts emerging from various investigation and the sources that are widening our understanding of human filariasis and hopefully this newer information can inform us further as how to more efficiently control, manage and hopefully eliminate the important human filariases.

2. Variations in form and presentation

In attempting to understand filarial infections one is presented with interesting and thought-provoking concepts. Aside from the phenomenon mentioned above of surviving and multiplying usually exclusively within the environment of a preferred host, and often in the vascular system—a preferential location also seen with trematode parasites (e.g., schistosomiasis)—filarial infections can present in different ways, which likely reflects underlying biological differences in host responses, worm stages and other factors. Firstly, there is clear clinical spectrum that ranges from those people who carry increasing parasitic loads with the parasites (microfilariae and

adult worms essentially) eventually dying at the end of their life expectancy. This is a situation where there appears to be a developed "tolerance" for these parasites, at least whilst they are alive and generally healthy. This form of the infection, due to the associated focal inflammatory reactions that occur as they eventually die, together with secondary effects (e.g., in OV pruritic irritation and consequent damage from self-scratching), which over a long period of time causes the associated tissues and affected organs to slowly degenerate. In OV this results in the often shown picture of a prematurely aged and atrophic skin, and in LF one sees slow chronic damage to the kidney and other highly vascular structures. At the other end of the clinical spectrum is a highly active condition centred around, at least in OV, very active microfilarial destruction with associated inflammatory events—this is seen in the condition known as "reactive oncho-dermatitis" (ROD) or "sowdah". It has been shown that ROD patients have very strong T-cell based immune responses to *O.volvulus*, whereas those infected people with the steadily increasing parasite load, the degenerative form of the disease, do not have such active T-cell responses. Thus, there is a clinical spectrum that is paralleled in many ways by a corresponding immunological spectrum.

Another variation that exists in filarial infections relates to the host tissue's responses to the different parasitic stages, most being known about the two stages that can be more easily identified in infected people, i.e., the adult forms and microfilarial stage (L1) (**Table 1**). In addition, the host reactions to each of these two stages can be different, and it is probable that changes in the biological status of each of these, or perhaps the host's immunological recognition of these specific stages, are the basis for these differences. Live adult worms appear from histological studies to reside in the tissues with only a minimal cellular response adjacent to at least most for their external surface. Two exceptions occur to this status: firstly, it is very common to find in the tissues associated, although usually not directly in apposition to these adult worms, substantial organised aggregates of lymphoid cells and plasma cells. This indicates in all likelihood that the presence of the adult worm, or at least significant components of this stage, is well recognised by the immune system, although the worm appears to manage to avoid being attacked by host responses through immuno-modulatory mechanisms. Observations in the bovine equivalent of human OV, *Onchocerca gutturosa*, where the female adult worms lie in a serpentine fashion in the epi-ligament membranes lining the nuchal ligament in cattle—the only cellular reactions associated with the live adult worms are again lymphoid cellular aggregates; however, in this case these are located adjacent to the vaginal opening of the female worms suggesting that material emerging from the worms's uterus (which maybe be uterine fluids, microfilariae or microfilarial components) are involved in the induction of this host response. The second major form of observable tissue response to adult worms is that associated with degenerating, or essentially non-viable, adult worms; it should be noted that the definition of nematode viability, and indeed the definition of a live versus a dead filarial worm, is controversial [5]. The cellular responses to degenerating adult filaria is characterised by the typically components of a chronic inflammatory response—e.g., macrophages of different morphologies, and in these cases, eosinophil leucocytes; this is parallel to a classical "foreign body" response in pathological terms. The latter response can be interpreted as resulting from the lack of any immuno-modulatory activity being shown by the now inactive adult worm.

The other easily identified parasitic stage, the microfilariae, also is associated with two different tissue reactions: either being alive and free from any cellular reaction, or in contrast degenerating and eliciting very active eosinophil dominant cellular reactions—the latter occurring, for example after the administration of microfilaricidal

agents such as DEC and ivermectin. It is thought that when microfilaria emerge from the uterus they change their surface composition which may protect them from host attack [2]. Treatment with microfilaricidal agents probably alters the capability of microfilaria to avoid the host's attack; this is likely the case with the function of ivermectin [6].

Likewise, with LF there is a dramatic range of responses seen clinically, although the mechanisms at play behind this variation are much less clear than those evident in onchocerciasis. There is relatively little data available in humans on the mechanisms behind the variations in those infected individuals that develop clinically obvious lymphoedema or hydrocoele, and those who do not. Suggestions for this difference in clinical presentation have been proposed and these include possible differences on host genetic type, differences in immunological history, and the more general overwhelming of the host's tissues natural ability to recover and absorb the pathophysiological stresses that result from infection and disturbed lymphatic drainage.

3. Changes in our understanding of the pathobiology

The location of filarial worms within the body are thought to be well known and accepted, however it would be judicious to emphasise that our current understanding of this is often based on general assumptions. The adult worms in OV are in general thought to be almost exclusively found in sub-cutaneous tissues, however it should be noted that very few autopsies that have specifically searched for adult worms. The autopsies that have been carried out revealed that adult worms can be found deep in the thigh muscles, in the fascia close to the femoral bone; this location, if it is common, lessens the value of using palpable sub-cutaneous adult containing nodules as an indicator of an individual's paradise load. Another recent finding that questions current thinking has shown that it quite possible that *O.volvulus* migrate and die in lymphatic vessels, those of the dermis, rather than moving in the supporting connective tissue, as was previously presumed [7]. This would support a general concept that virtually all filarial parasites reside in the vascular system. Such a generalisation still needs additional confirmation, especially for filariae such as loiasis, but as histological advances in identifying lymphatic anatomy continues improve this should indeed be possible.

Similarly, with regard the effects of adult LF worms there is a need to adjust long-held understandings. For many years it has been the generally acute concept that adult LF parasites "pack and block" lymphatics inducing lymphoedema. In truth, the complete opposite occurs, with the adult worms stimulating endothelial proliferation and very extensive enlargement of the lymphatic vessels (**Figure 1a** and **b**), rather than physical blockage by these parasites. It is this gross enlargement and expansion of the vessels that leads to their inability to keep the lymph fluid moving forward due to valvular insufficiency; thus, leading to lymph stasis and consequently decreased ability of the dermal tissues to protect the limb and keep it healthy.

The role of host immuno-protective mechanisms in filarial infections is still also not well understood. Histopathological observations in both humans and a rat model provide interesting indications that there is an inflammatory response in the lymphatic walls where the adult worms are residing (**Figure 1a** and **b**) [8]. Experimental studies in rats with secretions from the adult filarial worms showed that the macrophage cellular component of this perivascular host reactions is a likely an important player in the production of factors such as vascular endothelial growth factor (VEGF)—that are known to be elevated in filarial patients—are possibly involved

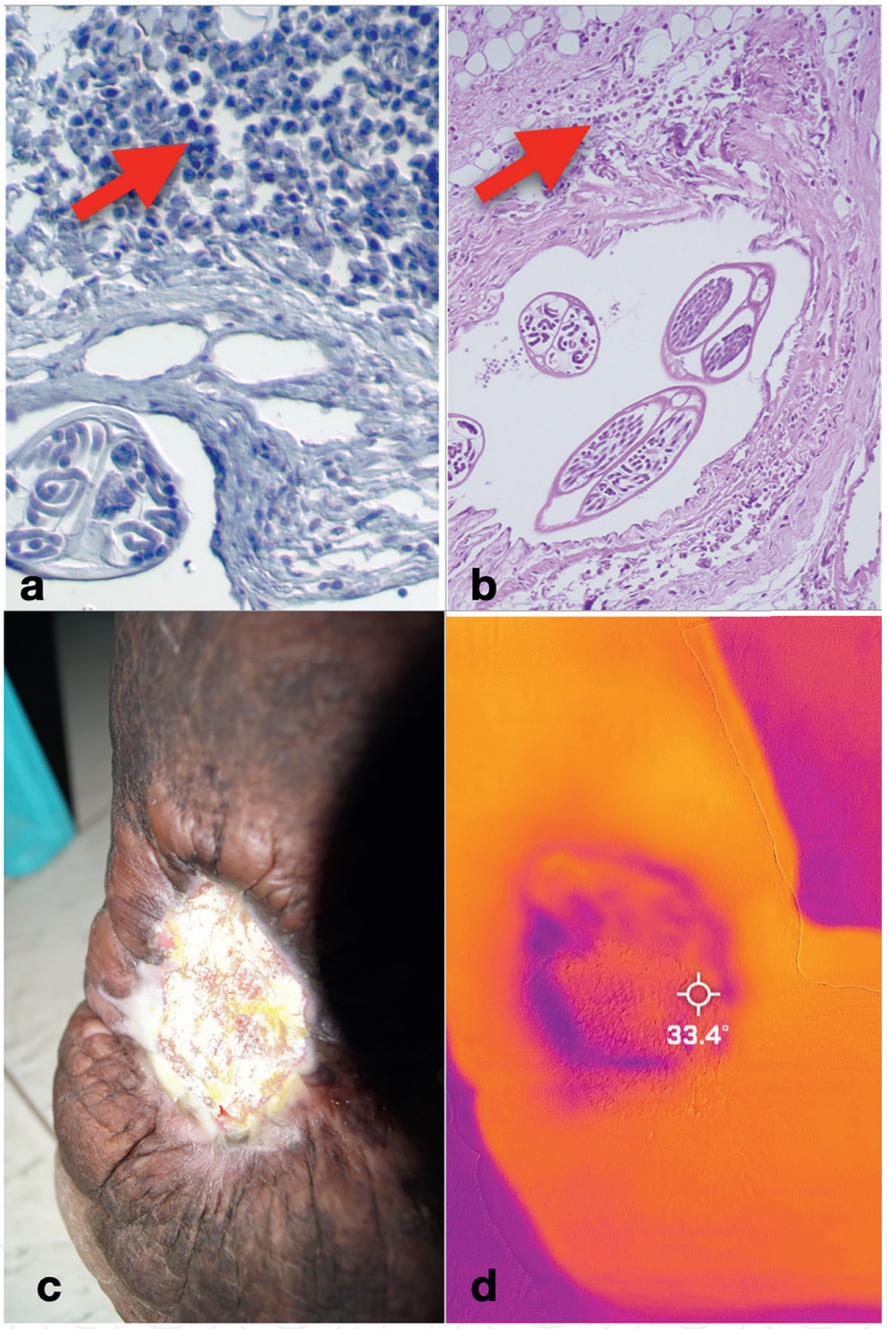

Figure 1.
Filarial infections and consequences; (a) Organised lymphoid aggregates in tissues associated with adult Onchocerca volvulus; (b) Reactive cells in the walls of the lymphatics carrying Brugia sp. adult worms; (c) Chronic inflamed wound in a lymphoedematous leg; and (d) Thermographic image of the area shown in c. showing temperature differential that shows areas of the wound that are actively inflamed (darker areas).

in the dramatic lymphatic wall proliferation that is a hallmark of this infection [9]. It is also interesting to note that the tissue reaction that is seen around dead adult *Wuchereria* worms that form "nodules" that often are attached to the internal walls of the affected lymphatics is very similar to that seen around the degenerating adult worms in the sub-dermal nodules of OV. Thus, suggesting the pathological mechanism at play with dead adult worms are similar between parasite species.

There is also support for secondary infections as a major contributor the progression, and perhaps a role in the initial development, of LF. The effectiveness of

bacterial and fungal control achieved with the skin hygiene self-care protocol for lymphoedema patients being the major piece of evidence presented to support this contention. It is likely though that the development and progression of lymphoedema has a complex aetiology that includes secondary infections, a parasitic component, certainly in the early stages, and also an important contributor in the marked diminution of the skin and its supporting tissues to be able maintain homeostasis and protect the affected area against external stresses and insults. Understanding the components involved in the pathogenesis of lymphoedema and associated dermal changes would likely greatly enhance the search for much needed new treatments.

Understanding which are the active components of filarial worms that stimulate inflammation, as well as which are the events and mechanisms associated with the prevention of these unwanted reactions, is central to developing better management of these infections. It is likely that microfilaria, and probably other components released from the adult female worm's uterus, stimulate active responses in the host. This may be explanation for the cellular responses seen in tissues adjacent to the uterine opening mentioned earlier. In addition, observations in animal models where the uterus of adult filarial worms have been damaged or blocked, significant cellular reactions do not occur in the tissues where these adult worms reside implying that the uterine components (which include microfilariae, eggshells, etc.) are causes of inflammatory responses. It is important here to mention the role of the common filarial endosymbiont, *Wolbachia*, that is present in at least some filariae (including LF and OV); this organism has been often defined as the major inflammatory component of these parasites. These organisms are indeed an important stimulatory component of these worms but it likely that components other than the endo-symbionts also elicit significant host responses and also contribute to the reactions that occur when these parasites degenerate and release their contents. Another finding that has requires better definition relates to the presence of high levels of circulating immune complexes in at least OV patients [10], and whether these high levels contribute to the immuno-modulation occurring in this disease.

When attempting to understand the host-parasite interactions of an infection it is important to observe the changes and effects as the infections develop in naive individuals (e.g., children and expatriates). Children born and growing up in onchocerciasis endemic areas appear to mount active microfilarial destroying responses that keep the loads of active detectable microfilariae low unit about 7–8 years of age after which the dermal loads begin to significantly increase [1]. This increase likely reflects the mounting ability of the parasite to modulate the host's protective responses against this parasite. Visitors to endemic areas, at least OV endemic areas, who become infected often show acute clinical dermal presentations that reflect reactions to the microfilariae present in their dermal tissues, and these can be quite severe, and these also likely reflect the presence of an active host reaction to the invading parasite.

4. Enhancing program implementation and assessment

An important area that could greatly assist both the OV and the LF programs is to understand the clinical and social effects of these infections, and the current approaches to treatment, have on those individuals affected and on their communities. Monitoring clinical changes over time is a very important approach that has not

commonly been carried out. Documenting change in the disease has several valuable outcomes—aside from promoting better individual patient management, showing a reduction in disease has important advocacy implementations for the global elimination program for OV and LF. An additional indicator of success is to monitor the appearance of new cases, where a reduction and an absence reflects the achievement of a successful anthelminthic program.

One of the major challenges to one of the required goals of the GPELF is to provide care to all those suffering from the often devastating two major clinical effects of this infection, i.e., firstly, lymphoedema and dermal pathology (LDP), and secondly hydrocoele (HC) [11]. The WHO has recommended effective protocols for these two conditions—removal of the parasitic cause and a package of skin-focused self-care procedures for lymphoedema and surgical intervention for HC. Registering and training LDP patients, many of whom often live in rural locations that do not have easy access, is challenging. In addition, these patients need to continue their self-care for long periods of time, if not for the remainder of their lives. Hydrocœlectomy surgery, however, is essentially a single event with over 80% success with non-recurrence of the HC, and thus is in managerial terms easier to implement in national programs and is relatively easy to quantitate and report. National programs therefore tend to focus on implementing the surgical component of the morbidity arm of the global efforts against LF rather than lymphoedema care.

As the chemotherapeutic arm of the LF elimination program, i.e., the mass distribution of anthelminthics, is essentially a procedure that should be completed in 5–8 years, and as many LDP patients will need to carry out their self-treatment activities long after the man anthelminthic phase has ended, it has been recommended that LF patient care be integrated in the public health services of endemic countries [11]. This is an appropriate managerial approach but in reality, this is turning out to be difficult to achieve, partially as medical care for a long term, largely chronic, condition that is not immediately life threatening is usually not a high priority for national medical administrations. Thus, a major challenge the national LF Programs must address, in addition to the initial establishment of a LF MMDP program (i.e. Locating LF patients, and making appropriate care available), is to encourage and ensure that LDP patients maintain their self-care over a long-period of time. Understanding how to do this one of the major questions that those wishing to make the global program a complete success need to address: how do we support LDP patients to keep employing the skin care self-care package? Understanding why these patients do not continue their self-care activities, and what support mechanism can be developed to assist their continuance in long-term self-care, are two essential questions that need to be addressed in this goal. Similarly in importance is the development of improved methods to demonstrate any positive clinical effects of these global treatment and elimination efforts on those affected - such as the reduction in the occurrence of new cases, and improvement in existing pathology, would serve well to promote the Program's success.

It is important that modern tests and procedures are developed for assessing filarial patients in routine and special investigations, although it is realised that many, if not most, OV and LF patients reside in areas of the world where medical services are extremely weak if existent at all. Most of the current parameters used for assessment are external in intervention and general in information. It is also likely that approaches that reveal more information about the changes taking place in deeper tissues and organs will be very informative to achieving a better understanding of these

infections and their consequences. As mentioned above, it is notable that despite the number of people infected and affected by this infection there are so few documented autopsies available. Ultrasound is commonly used to visualise infected lymphatics and subcutaneous onchocerca nodules, and newer techniques such as optical coherence tomography and Nuclear Magnetic Resonance (NMR) have been used occasionally in investigations in OV or LF.

Externally based parameters are still the most practical of approaches to assess filarial patients in most locations across the endemic zones of the world. It has been found in practice, in our work in Tanzania, that it is important to assess the status of a patient from a holistic point of view, i.e., incorporate together a range of signs, symptoms and appropriate aspects of daily action and mobility. Using a single parameter to assess status or change in status has not been found to be robust enough for carrying out comparisons, either longitudinally in a single patient, or between patients. In OV, there are tools that can be used for both ophthalmologic disease and dermal disease: the presence and change in punctuate keratitis is a useful indicator for the eye, and scoring of the presence and degree of the major dermal changes associated with oncho-dermatitis foe assessing the skin.

With LF induced lymphoedema a common approach is to measure the size/volume of the limb enlargement; this done by either the impractical approach of water displacement, the use of tape measurements of circumferences at standard levels on the limb, or more recently using infra-red [12], or digital volume sensors (such as Lymphotech®) [13]. It should be noted, however, that changes in limb volume can vary considerably over the course of 24 hours, and it is not uncommon for patients who are generally improving to relate that their affected leg "does not weigh as much as it did," although there be no obvious detectable change in affected limb's volume. Incorporating as many quality-of-life parameters (e.g., mobility, duration of working in farms, etc.), are important to use along with the more classical parameters of the observable stage of lymphoedema and dermal change (using the standard described lymphoedema staging scales), and the occurrence of acute filarial attacks (AFA—i.e., increased limb swelling, draining lymph node swelling, feeling "feverish", and other signs and symptoms). It is useful to record not just the occurrence (the number) of acute filarial attacks but also their duration and severity—a reduction in AFA has been found to be a most useful parameter for demonstrating an individual's clinical improvement (**Figure 2**). Another useful tool is thermography to monitor temperature differences in active areas of the dermis [14] (**Figure 1c** and **d**). As this is a condition that stigmatises those it affects, it is important to take steps to address both the stigma the patient feels and any negativeness expressed by the community members where they reside. Active provision of care to those affected in an endemic community affected, and the visibility of seeing patients' improvement, can go a long way to reduce the overall problem of stigma—and secondarily enhance trust in the national program's activities often resulting importantly in higher mass drug administration compliance.

5. Major questions remaining

Understanding the pathobiology of filarial infection is challenging, given their many unique characteristics such as their host specificity and ability to avoid natural defense mechanisms, but this is an intellectually exciting goal, one that is likely to have valuable practical consequences. It is important when addressing this challenge

a. FREQUENCY IN OCCURRENCE OF ACUTE FILARIAL ATTACKS

Reported attacks in the 12 months prior to MDA/Self-care	1.6	0.1 - 2.2
Reported attacks in the period 12-24 months after MDA/Self-care	0.2	0 - 0.3

b.

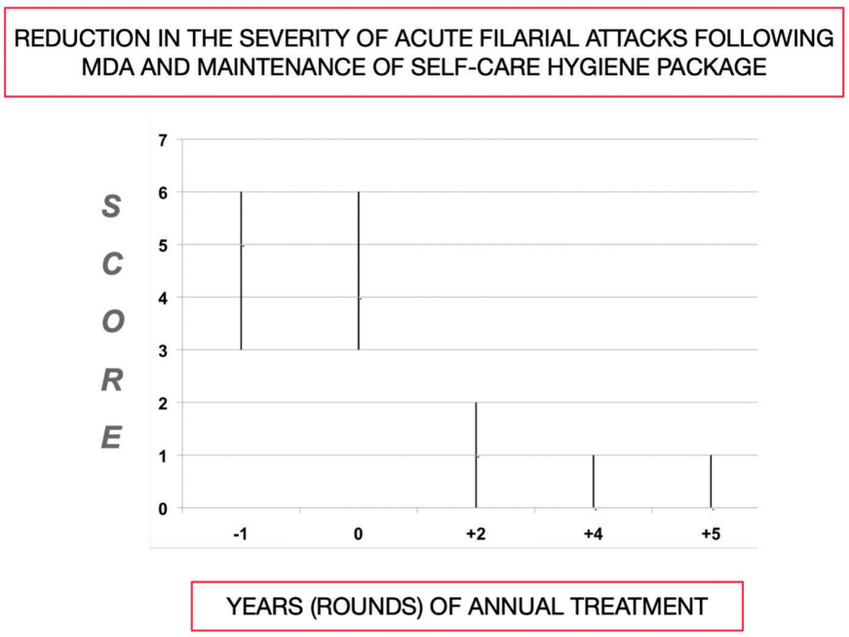

Figure 2.
Acute filarial attacks (a) Change in frequency of filarial attacks in 147 lymphoedema patients after 2 years of receiving the anti-filarial chemotherapy and implementing the recommended self-care hygiene package; and (b) Changes in the clinical presentation of acute filarial attacks in 47 individuals with lymphoedema (47 individuals) following the treatment regime (the assessment score was based on frequency, duration, and severity of the attacks).

to taking a wide approach and to not get over-focussed on specific findings without considering the whole spectrum of the parasite-host interaction, and to keep the major goals in mind—e.g., detection, safe treatment, and reduction in endemicity. A selection of major questions reaming is presented in **Table 2**.

As presented in this discussion it is important to get more data and information about the lesser investigated areas of filarial infections, especially in areas related to understanding the mechanisms in the host-parasite interactions that allow these infections to survive and multiply in sensitive tissues. Currently most of the effort, both politically and fiscally, is being placed on achieving the goal of disease elimination or at least reduction through wide distribution of chemotherapy with some additional supportive approaches (e.g., vector control). A common argument presented is that we do not need to have deeper knowledge of an infection that is being successfully controlled, and now eliminated, from individual countries. In the long-term this may be a valid statement, but we are long way from success extending across the whole OV and LF endemic world, and in addition these drug administration programs are extremely long in duration which is costly. Improved diagnostic tools, more effective means of treating areas

Area of focus	Relevance
What are the differences and commonalities between the different filariae?	Can we make assumptions across filarial sp.?
How do filarial parasites modulate the host's immune system?	Aid in developing better therapies and reduction in parasite loads
Are there unique species specific components that could be used for minimally invasive diagnosis?	Diagnosis and epidemiology
What are the components of filariae that induce inflammatory reactions?	The developing of improved supportive treatments
What are the roles of secondary factors In each filarial disease?	Understanding the complexity if filarial clinical disease
How to best detect the presence of filarial parasites infection in deep tissues?	Improve diagnosis and monitoring of treatment
What is the best practical method to detect and estimate the presence of fertile/actively reproducing filarial parasites?	Central to breaking transmission

Table 2.
Major areas that could be investigated to provide a more detailed information on the patho-biology and detection of the major human filarial infections.

of persistent infection, and more effective treatments (chemotherapeutic agents), could lead to program success much faster than is currently occurring. Addressing any of the questions such as those described in this current discussion would likely contribute positively to improving the activities needed for elimination in many ways (**Table 2**). For example, increasing advocacy for continuing the drug distribution program with donors and recipients by showing clinical improvement in those affected would likely be most advantageous, as would improving the tests used for the detection of cases that are essential for epidemiological assessment that define success.

Although in recent times our understanding of filarial infections has indeed improved, and some fundamental misunderstandings corrected, the emotive classical images of clinical filariases—the grossly swollen limbs, enlarged genitals, and the blind being guided by young children, are unfortunately still often regarded by the public as the current status of these infections. Hopefully this public view will change to one that embraces the success of the recent efforts to understand and reduce this devastating disease. The fact that many LF patients are now receiving treatments that does indeed reduce their morbidity needs to be more generally known. In addition, the observation that in recent years the appearance of new cases of onchocerciasis-induced blindness is now very much frequent needs to be better understood but the public health community.

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