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REVIEW

Progress towards elimination of lymphatic filariasis in the Eastern Mediterranean Region

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Lymphatic filariasis (LF), a neglected tropical disease, is targeted for global elimination as a public health problem. This article reviews the history of LF control and elimination activities in the countries of the World Health Organization's (WHO) Eastern Mediterranean Region (EMR) over the last 2 decades. In 2000, the estimated at-risk population in EMR countries was 12.6 million people, accounting for approximately 1% of the global disease burden. Of the 22 EMR countries, 3 countries (Egypt, Sudan and Yemen) were LF endemic and the disease was suspected in 4 other countries (Djibouti, Oman, Somalia and Saudi Arabia). After almost 2 decades of implementing sustained control and prevention measures, Egypt and Yemen were successfully validated by the WHO as having achieved the elimination criteria in 2017 and 2019, respectively. In 2018, Sudan completed mapping of LF, reaching 26.2% geographical coverage where mass drug administration (MDA) is required and is scaling-up MDA. Extensive epidemiological assessment indicated the absence of LF transmission in the four suspected countries and no MDA required. Challenges faced during the elimination and post-elimination phases are described and discussed.

Introduction

In 2000, the World Health Organization (WHO), in response to World Health Assembly (WHA) Resolution 50.29,[1] launched the Global Programme to Eliminate Lymphatic Filariasis (GPELF).[2] The GPELF strategy has two components: to stop the spread of infection (interrupting transmission) and to alleviate the suffering of affected populations (controlling morbidity). The Office for the Eastern Mediterranean Region (EMR) of WHO comprises 21 member states and Palestine (West Bank and Gaza Strip), with a population of nearly 583 million people. Of these, three countries (Egypt, Sudan and Yemen) are known to be endemic for LF and the disease was suspected in four other countries (Djibouti, Oman, Somalia and Saudi Arabia).[3] This article reviews the history of LF control and elimination activities in the countries of the EMR over the last 2 decades and sheds light on challenges faced during the elimination and post-elimination phases.

Elimination of LF from Egypt

History of LF control

In Egypt, LF caused by infection with nocturnally periodic *Wuchereria bancrofti* has been known to be endemic since ancient times.[4] Entomological studies have indicated that *Culex pipiens* is the dominant vector mosquito.[5] During the 1950s and 1980s, the Ministry of Health and Population (MoHP) conducted nationwide surveys to map LF in rural and urban districts, revealing that LF was focally endemic in rural areas.[6,7] LF control was based on selective treatment of microfilaremic (MF) subjects with a 12-d regimen of diethylcarbamazine (DEC; 6 mg/kg/day). In 1996, the MoHP changed its anti-LF strategy to selective treatment with single-dose DEC (6 mg/kg), as it was shown to be equally effective.[8] Vector control relied on eliminating mosquito breeding sites through larviciding and residual house spraying.[9] Such activities were carried out in the most endemic villages in the eight known LF-endemic governorates (Assiout, Dakahlia, Gharbia, Giza, Kafr El Sheikh, Menoufia, Qalyubia and Sharqia). However, due to time and budget constraints, LF surveys combined with selective DEC treatment could not be maintained on a yearly basis in all endemic villages.

The national LF elimination programme (NLFEP) in Egypt

In 2000, Egypt was among the first countries to join the WHO global efforts and initiated a national programme to eliminate

Table 1. Summary of data for all MDA rounds implemented in Egypt during 2000–2013

MDA round (year)	Governorates, n	Districts, n	IUs (villages)[a], n	Target population (million)	Mean MDA coverage, %
MDA-1 (2000)	7	25	161	1.9	90.0
MDA-2	8	27	178	2.4	93.0
MDA-3	8	27	179	2.5	95.2
MDA-4	8	27	181	2.6	93.2
MDA-5 (2004)	8	27	181	2.7	93.2
MDA-6[b]	5	14	45	0.8	91.7
MDA-7	5	10	28[c]	0.5	89.7
MDA-8 (2007)–MDA-14 (2013)	5	10	29[d]	0.6	87.6

[a]More IUs were added in 2000–2007, according to LQA mapping surveys, using the ICT card.
[b]After five rounds, MDA was stopped in 149 villages (92.5%). The sixth round of MDA, implemented in January–February 2006, included 45 villages: villages failed post-MDA-5 evaluation (n=12), villages received less than five MDA rounds (n=20) and newly included villages (i.e. started the first round of MDA; n=13).
[c]MDA was stopped in 17 villages (received the first MDA in 2001). The 28 IUs included villages that failed the post-MDA-5 evaluation (n=12) and villages that received less than five MDA rounds (n=16).
[d]In 2007, the last IU was included to start the first round of MDA. Thus the total number of IUs under MDA was 29, all of which were included until the last MDA round implemented in 2013.

LF as a public health problem, decreasing MF prevalence rates to <0.1%. The NLFEP was based on mass drug administration (MDA) of an annual dose of DEC (6 mg/kg) in combination with albendazole (400 mg). The programme aimed to achieve an MDA coverage rate of about 80% of the total population of the target implementation units (IUs). The village was chosen as the IU and all villages with MF or an antigen prevalence rate of ≥1% were included in the NLFEP. In 2000, there were 4132 villages in Egypt (1996 census). Of these, 522 villages were suspected LF-endemic areas based on MoHP data (326 villages) or key informant questionnaires (196 villages). Based on MoHP data (MF ≥1%), the first MDA round was conducted in 161 IUs in 2000 (Table 1). Additional IUs were included in subsequent MDA rounds based on lot quality assurance surveys (LQASs) conducted in 361 villages in 2001 and onward. For LQASs, 250 schoolchildren (15–18 y old) from high schools serving one to three adjacent villages were randomly selected and tested using the immunochromatographic test (ICT).[2] The total reached 195 IUs, with the last IU included in 2007, and the at-risk population reached approximately 3.7 million people.[10] The epidemiological coverage for all MDA rounds was ≥80% (Table 1). A research team at Ain Shams University confirmed that MDA greatly affects variables related to infection (microfilaremia and circulating filarial antigenemia prevalence rates) and transmission (antifilarial antibodies in young children and mosquito infection rates).[11] Surveys to stop MDA were conducted based on WHO guidelines in 2005[12] and 2011.[13] Antigenemia levels found in schoolchildren during transmission assessment surveys (TASs) in 166 IUs approximately 10 years after stopping MDA were 0% (Table 2). Note that due to budget constraints, unavailability of resources for procurement of ICT and TAS operational costs, TASs could not be conducted for several years. In 2017, the last TAS, conducted in an additional 29 IUs, indicated 0.1% antigenemia and 0% microfilaremia. Note that in the last TAS, filariasis test strips (FTSs), a second version of and more sensitive than the ICT, were used.

It is worth mentioning that surveillance after TAS-3, based on detection of MF, did not reveal any resurgence of LF in any IU. However, in 2016, such surveillance identified a small focus of LF with MF prevalence of 2.0% in Atris village, Giza governorate, a location that had not been included in the national MDA program. Currently this village and its surroundings are being annually treated by the triple-drug regimen, according to the WHO updated guidelines.[14]

In 2015, the registration of chronic LF patients was updated to 1472 lymphedema and 18 hydrocele patients. Morbidity management and disability prevention (MMDP) and training on self-management was provided to lymphedema patients, together with drugs and information booklets. Hydrocele patients were referred to local general hospitals for surgery. The NLFEP made excellent progress due to strong collaboration between different ministries, through intensive training and supervision and through the use of advocacy for mobilization of endemic communities.

Thus, after more than a decade of sustained effort, Egypt met the WHO criteria for successful elimination of LF as a public health problem. In December 2017, WHO validated Egypt as the first country in the EMR to successfully achieve elimination.[10] As noted by a member of the Dossier Review Group; 'A huge amount of credit should go to this program and its academic collaborators for strengthening the evidence-base not only for the Egyptian program but for the Global Program as well'.

Elimination of LF from Yemen

In Yemen, although chronic LF cases have been detected by health workers, there are no historical records of the disease in the literature. However, 'Sowdah', a localized form of onchocerciasis, with no records of eye complications or blindness, is

Table 2. Summary of different TASs conducted in Egypt during 2005–2017

	MDA stopped based on WHO guidelines of 2005[a]					
					ICT	
Date	Examined IUs, n	At-risk population, n	IUs passed, n (%)	IUs failed, n (%)	Tested, n	Positive, N
2005	161	2 783 985	149 (92.5)	12 (7.5)	9000	1[b]
2006	17	198 924	17 (100)	0	3000	0
		MDA stopping based on WHO guidelines of 2011				
2011	29[c]	618 193	29 (100)	0	3088	0
2014[d]	166	3 043 164	166 (100	0	9619	0
	29	630 680	29 (100)	0	3188	0
2017	29[e]	655 655	29 (100)	0	3417	2

[a]Equivalent to TAS 1.
[b]One cluster (12 IUs) failed the MDA stopping exercise.
[c]The number includes 12 IUs that failed TAS 1 (2005).
[d]TAS 3 conducted for 166 IUs, TAS 2 for 29 IUs.
[e]The FTS was used. The cut-off was 18 children and all IUs passed the TAS. The two children were MF negative and were treated by a dose of the drug combination.

endemic in certain parts of the country. In 2000, filariasis due to *W. bancrofti* was recognized as a public health problem in mainland Yemen and Socotra Island and *Culex quinquefasciatus* was found in 2005 to be the major mosquito vector of the disease.[15,16]

In 2000, the national Programme for the Elimination of Lymphatic Filariasis (PELF) was established by the Ministry of Public Health and Population. During 2000–2001, a nationwide mapping survey was conducted to determine the geographical distribution of LF in all 22 governorates, including Socotra Island. LQASs using the ICT, based of detection of LF antigenemia, were conducted. LF was found to be focally endemic in eight districts (in seven governorates, including Socotra Island), with antigenemia prevalence ranging from 2 to 40%. The subdistrict (Ozla) was chosen as the IU for MDA. During 2002 and 2009, MDA (ivermectin and albendazole) was conducted in the eight districts, covering an at-risk population of >100 000. By 2006, seven IUs had completed five rounds of MDA, and all but one had reached the criteria for stopping MDA. After three more annual rounds of MDA during 2007–2009, supplemented with application of expanded polystyrene beads to mosquito-breeding places as a vector-control measure,[16] the criteria were reached in the remaining IUs and MDA was stopped.[17] In 2013, 4–6 years after MDA was discontinued, a TAS was conducted. None of the schoolchildren tested was ICT positive. The third TAS was conducted in 2016 with the FTSs, which also gave negative results.

For MMDP, leprosy healthcare workers in national leprosy elimination programme (NLEP) clinics, located all over the country as part of the public health clinics system, have been treating people with lymphedema since commencement of the programme in 2000. A total of 610 lymphedema patients (379 males and 231 females) and 31 hydrocele patients are recorded. The NLEP personnel have been trained to care for chronically affected patients, who receive the minimal package of healthcare for lymphedema management, healthcare aids, drugs and information booklets.

In 2019, after almost 2 decades of sustained disease control and prevention measures, Yemen was validated by the WHO as achieving elimination of LF as a public health problem.[18] This was a landmark accomplishment in a particularly challenging environment.

The Sudan LF elimination programme (SLFEP)

In Sudan, LF caused by infection with nocturnally periodic *W. bancrofti* has been known since the 1930s.[19] During the 1960s–1970s, a few spot surveys carried out in parts of West Kordofan, South Kordofan and Darfur states reported MF prevalence ranging from 21.9 to 30.6%.[20] Other reports indicated that LF is endemic in an additional four states (Blue Nile, South Darfur, South Kordofan and West Kordofan).[3,17] It is noteworthy that Sudan is co-endemic for onchocerciasis.

The SLFEP was established by Sudan's Federal Ministry of Health. In 2016 the SLFEP completed mapping of LF in all 18 states of Sudan. The district (locality) was chosen as the IU. Of a total of 185 localities, LF is focally endemic in 61 (32.4%), distributed in 13 states, with a total at-risk population of approximately 9.7 million.[21] The SLFEP started MDA (ivermectin and albendazole) and the geographical coverage, programme coverage and national coverage were 26.2% (16/61), 78.4% (1 713 149/2 185 864) and 17.2% (1 713 149/9 965 945), respectively, in 2018.[21]

LF in other EMR countries

LF has been suspected in Djibouti, Somalia, Saudi Arabia and Oman.[17] In Oman, 15 LF cases were reported during 1991–2001;[22] most cases were classified as imported based on the patients' staying in LF-endemic countries. Oman has a high

expatriate population representing 46% of entire population,[23] many of whom are from LF-endemic countries such as Egypt, India and Sri Lanka. In addition, a study carried out in 2001 reported LF antigenemia (ICT) prevalence of 4.2% among Indian expatriates.[24] Therefore, in 2010, the Ministry of Health carried out intensive LQASs based on key informant questionnaires, followed by ICT surveys in high school children (17–18 y of age) from eight suspected transmissible districts. All tested students were negative for circulating *W. bancrofti* antigen, revealing that LF is not endemic in Oman.[25]

Similarly, epidemiological investigations have revealed that MDA is not required in Somalia,[26] as FTS surveys in 10 geographical regions (2016–2017) indicated a prevalence of 0.3% (Ministry of Health, unpublished data) in Djibouti[27] and Saudi Arabia.[28]

Challenges faced during the elimination and post-elimination phases

During the elimination phase, conflict and human migrations are key social determinants. Although the LF-endemic population in Egypt is stable due to agricultural practices, human migration represents a challenge in Sudan and Yemen. Additionally, since 2011, the three LF-endemic countries have undergone sweeping political changes with major reforms that had an impact on the sustainability of LF elimination activities. Also, political instability has led to some temporary backsliding in maintaining a strong commitment from senior and local health officials. In addition, a lack of committed international partners has resulted in considerable economic constraints; e.g. >75% of the NLFEP costs are provided by local Egyptian funds[29] and in Yemen the LF programme, since its inception, was fully integrated with the Leprosy Programme, which is supported by international agencies.

The main objectives of the post-elimination phase are to continue care of chronic filariasis patients and maintain surveillance to detect hidden endemic foci or LF recrudescence. Ideally post-elimination surveillance should be based on a sensitive diagnostic tool, assessment of circulating filarial antigen by FTSs. However, currently there are no FTSs donated for such surveillance activities and, due to budget cuts, disease elimination programmes are unable to purchase FTSs. Therefore, detection of MF in night blood is the only available diagnostic tool.

In addition, people with lymphedema must have access to continuing care throughout their lives, both to manage the disease and to prevent progression. Therefore patients were provided with a booklet, in the local language, for self-care in morbidity management, with kits containing soap, antibiotics, paracetamol and gauze cloth, free of charge. In the post-elimination phase, however, due to budget cuts, patients were advised to buy the kit components thereafter.

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