

EDITORIAL

LYMPHATIC FILARIASIS AND THE GLOBAL ELIMINATION PROGRAM

Rahmah Noordin

Institute for Research in Molecular Medicine (INFORMM), Suite 110, Eureka Complex,
Universiti Sains Malaysia, 11800 Penang, Malaysia

Key words : *Lymphatic filariasis, elimination program*

Lymphatic filariasis (LF) affects ~ 120 million people worldwide and ~1.1 billion people are at risk of acquiring this infection in 83 countries. It has been identified by the World Health Organization (WHO) as the world's second leading cause of permanent disability and a major impediment to socioeconomic development, thus a major contributor to poverty of the affected countries. However lymphatic filariasis often is given low priority in health care systems of developing countries, as compared to diseases that cause mortality. Thus it is listed by WHO as one of the main diseases under the Neglected Tropical Diseases (NTD).

Lymphatic filariasis is caused by three species of filaria namely *Wuchereria bancrofti*, *Brugia malayi* and *Brugia timori*. The first species causes bancroftian filariasis and is responsible for 90% of the infection; while the latter two species cause brugian filariasis which account for 10% or ~13 million infections. *Brugia* is the predominant species in Asia namely in Indonesia, South India, South China, Thailand, Malaysia, Vietnam, Philippines and South Korea. In Malaysia, endemic areas are found in the states of Sarawak, Sabah, Terengganu, Kelantan, Pahang, Perak, Selangor and Johor. The main endemic areas for *W. bancrofti* are in India, Africa, South America, parts of Middle East and the Pacific islands.

The infection is transmitted by several species of mosquitoes. After a blood meal, third stage larvae (L_3) of the parasites are released from mouth parts of mosquitoes and crawl into the wound. They enter the lymphatic circulation and migrate to lymph nodes and lymphatic channels. There they develop into male and female adult worms, and after mating, the females produce microfilariae (mf). The mf enter the blood circulation and are taken up by mosquitoes when they feed on the infected humans. In the mosquitoes, the mf develops into L_3 and the life cycle

continues. The period between human infection and mf detection ranges from 3 to 6 months and mf are produced for 2-3 years; while adult worms live for about 5-10 years.

There is a wide range of manifestations of lymphatic filariasis, these include fever, malaise, lymphatic and renal damage, inflammation of the lymphatic nodes and channels (adenolymphangitis), lymphoedema, hydrocoele, chyluria and elephantiasis. The most chronic and obvious form of the disease is elephantiasis but this occurs in about ~10% of the infected people. Most infected people have subclinical dilated lymph vessels which tend to worsen slowly especially in those who strain their lymphatics due to their jobs or daily activities that involve long periods of standing or strenuous exercise. This dilatation tends to be irreversible so that after varying periods of time, later in their lives, these people may get acute attacks from secondary bacterial infections due to stagnation of lymph. Any associated diabetes mellitus or immune suppression due to other diseases will worsen the bacterial infections and make them more prone to septicaemia. Some individuals develop lung damage due to accumulation of mf in this organ in cases of occult infections, where mf is never found in the peripheral blood circulation due to the host allergic reaction ; a condition known as tropical pulmonary eosinophilia. Due to the generalized symptoms observed in the early phase of the infection and the poor sensitivity of the traditional detection method, many infected people are not diagnosed.

If an infected individual is diagnosed early, sufficient treatment by diethylcarbamazine (DEC) is quite effective to kill the adult worms. If the disease has progressed to a late stage lymphoedema or elephantiasis, DEC is no longer effective since at this stage the adult worms are already dead and other modes of treatment such as surgery is required.

The traditional/routine method to diagnose

brugian filariasis is by taking a sample of finger-prick blood at night and examining it under a microscope for presence of mf. In the day, most or all of the mf are hiding in blood capillaries of internal organs (phenomenon of periodicity). This traditional method severely lacks sensitivity (25%- 40% sensitive), thus missing many positive cases. This is due to the inability of the method to detect cryptic infections (before mf is produced and after mf ceased to be produced), single sex infections, occult infections and low levels of mf. PCR-based detection methods are very sensitive to detect low levels of mf, however it is not suitable for detection of cryptic, occult or single sex infections.

During the Fiftieth World Health Assembly in 1997, a resolution was adopted for elimination of LF as a public health problem by the year 2020. Elimination is defined by mf rate of <1% and <1/1000 infected children for five cumulative years. In 1998, WHO initiated a Global Program for Elimination of Lymphatic Filariasis (GPELF), with two main objectives namely: (a) interruption of active transmission through mass drug administration (MDA) of once a year, single dose, two-drug regimen with DEC and albendazole (or Ivermectin and albendazole) to the endemic population (at least 80% coverage) for at least five years; and (b) alleviation of disability by management of clinical cases. A global alliance (Global Alliance for Elimination of Lymphatic Filariasis or GAELF) comprising of donors, ministries of health of endemic countries and NGOs was formed to tackle the wide-ranging and complex process of science and practice in order to achieve the goals of GPELF.

The endemic countries in the world are at different stages of the elimination program. China has recently submitted the documents to WHO for the certification of elimination, while some countries in Africa has yet to carry out mapping of endemic areas. In Malaysia, the endemic areas cover a population of 1169610, comprising 139 *mukims* or implementation units (IU). By 2006, most endemic areas in Malaysia have achieved three rounds of MDA, and the target year for certification of elimination in this country is 2013.

There are two main reasons that GPELF has been viewed optimistically namely availability of good diagnostic tools and the demonstration that a simple two drug regimen once yearly can drastically reduce circulating microfilariae. The diagnostic tools are needed for accurate mapping of endemic areas, for monitoring activities, certification of elimination

and surveillance activities post-elimination. For bancroftian filariasis, a rapid antigen test is commercially available (Filariasis NOWTM, Binax, USA) for mapping and monitoring activities, but this test is considered not sufficiently sensitive for use in the phases of certification and surveillance post-elimination. For brugian filariasis, *BRUGIARapid*TM, a test based on detection of anti-filarial IgG4 (a marker of active infection) has been endorsed by the WHO Technical Advisory Committee for use in the GPELF. This test is a USM invention and is being commercialised by Malaysian BioDiagnostic Research Sdn. Bhd. Two other rapid tests have been licensed by USM to MBDr namely *WBapid*TM and *panLFrapiid*TM. The former would be suitable for use in the certification of elimination and surveillance post-elimination in bancroftian filariasis endemic areas. For areas with mixed infection (brugian and bancroftian filariasis) and for screening of foreign workers, *panLFrapiid*TM would be a very useful diagnostic tool.

Two major drug companies have pledge to provide free drugs for the program namely GlaxoSmithKline (albendazole) and Merck & Co (ivermectin). Poorer endemic countries also receives free DEC from WHO. These generous donations are pivotal in ensuring the success of the GPELF. However there remain many challenges faced by the program. These include 'donor fatigue', reduced treatment compliance as the program progresses and the inconsistent commitments of governments of endemic countries when faced with other problems that vie for the same resources. Availability of research funds are also dwindling due to the perception that active research is not necessary for a disease which is on the process of elimination. This perception needs to be corrected since active research must be carried out in tandem with the program to tackle the many difficulties that are bound to arise in such a massive undertaking and to provide continuous input of data to ensure that the program is on the right track.

Corresponding Author :

Prof. Rahmah Noordin Ph.D
Institute for Research in Molecular Medicine (INFORMM), Suite 110, Eureka Complex,
Universiti Sains Malaysia, 11800 Penang, Malaysia
Tel: + 604-6532881
Fax: +604-6567176
Email: rahmah@usm.my

References

1. WHO report, SEA-FIL-31, 2005
2. Report from Ministry of Health Malaysia (Dr. Che Abdullah Hassan, Program Manager of the National PELF)
3. WHO Annual Report on Lymphatic Filariasis 2003