

Urban lymphatic filariasis

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Abstract Lymphatic filariasis (LF) is a disabling and disfiguring disease resulting from a mosquito-borne parasitic infection. It is a major public health problem in many countries with a warm climate. Research and control activities have mainly focused on LF in rural areas where it also has its major impact. However, with rapid and unplanned growth of cities in the developing world, there is a need also to consider LF transmission and control in urban settings. Here, we review currently available knowledge on urban LF and the environmental and socio-economic basis for its occurrence. Among the three parasite species causing LF in humans, only *Wuchereria bancrofti* has been documented to have a significant potential for urban transmission. This is primarily because one of its vectors, *Culex quinquefasciatus*, thrives and proliferates excessively in crowded city areas with poor sanitary, sewerage and drainage facilities. For this reason, urban LF also often shows a marked focality in distribution, with most cases clustered in areas inhabited by the less privileged city populations. More knowledge on urban LF is needed, in particular on its socio-economic and human behavioural context, on the potential for transmission in regions where other LF vector species predominate, and on rapid methods for identification and mapping of risk areas, to provide a strong evidence base for its control.

Introduction

Recent decades have witnessed a tremendous increase in urbanisation worldwide, and in 2009, more than half of the world's population lived in urban areas (Leon 2008; Castro et al. 2010; Alirol et al. 2011). This proportion is expected to increase, with much of future urbanisation taking place in low-income developing countries. For example, in sub-Saharan Africa, the urban population has grown from about 10 % in 1950 to over 35 % now, and it is estimated to be more than 50 % by 2030. Urban growth is partly due to migration from rural to urban areas and partly to natural increase of the existing urban population, and most of the current growth takes place in small- and medium-sized cities (Leon 2008; Alirol et al. 2011). The rapid urban growth in developing countries, with limited economic opportunities, often results in the establishment and expansion of informal settlements and slums. These are areas where households lack access to safe water, adequate sanitation, sufficient living space, durable housing and security of tenure (UN-HABITAT 2006). Among other health consequences, such conditions provide favourable habitats for proliferation of disease vectors and for transmission of many of the so-called neglected tropical diseases such as soil-transmitted helminthiasis, schistosomiasis and lymphatic filariasis (Mott et al. 1990; Knudsen and Slooff 1992; Utzinger and Keiser 2006; Patel and Burke 2009).

Research on lymphatic filariasis (LF), a disabling and disfiguring mosquito-transmitted parasitic disease, has so far mainly focused on rural environments, where it also has its major impact. However, LF also has a potential for urban transmission, and urban LF was recently identified as one of the major future challenges for the current global efforts to eliminate LF as a public health problem (Addiss 2010; WHO 2010). Knowledge on the extent and epidemiology of urban LF, including the environmental, socio-economic and behavioural basis for its occurrence, is important for design and

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implementation of effective control in urban settings. Here, we review currently available knowledge on urban LF and the factors that facilitate its transmission, in order to provide an informed background for further studies and for addressing its control.

Human LF and its transmission

Human LF results from infection with three different species of mosquito-borne filarial nematodes: *Wuchereria bancrofti*, *Brugia malayi*, and *Brugia timori* (Simonsen 2009). The parasites are transmitted to humans when infected mosquito vectors deposit infective larvae onto the human skin. The larvae penetrate the skin and migrate to the lymphatic vessels where they develop into male and female adult worms over a period of months. The mature and fertilised female worms release large numbers of minute microfilariae (mf) which circulate in the blood. Mf ingested by a vector during a blood meal will develop to infective larvae in about 10–14 days. These migrate to the mosquito's proboscis and may then be transmitted to a human during a subsequent blood meal. The mosquito vectors thus play an essential role in maintaining the life cycle and dissemination of the infections. Various species of man-biting mosquitoes serve as vectors in different parts of the world, and vector species bionomics are important in determining the type of environment that can support transmission of the parasites.

B. timori infections are restricted to islands in Eastern Indonesia and are estimated to affect less than one million people (Fischer et al. 2004). The only known vector is *Anopheles barbirostris*, which mainly breeds in rural areas with intensive rice cultivation. *B. malayi* infections are more widespread in South and Southeast Asia (Ramachandran 1981) and an estimated 12 million people are affected. The main vectors are *Mansonia* spp., which are unique in that their larvae live in association with certain species of floating freshwater plants thriving in unpolluted waters. In more limited areas, *B. malayi* is also transmitted by *Anopheles* spp. Breeding of vectors for both species of human *Brugia* is thus essentially related to clean freshwater bodies in rural environments.

W. bancrofti is the most widespread lymphatic filarial parasite of humans, affecting more than 100 million people in Asia, Africa, Central- and South America and the Pacific (Simonsen 2009). Transmission is facilitated by a multitude of mosquito species belonging to the genera *Aedes*, *Anopheles* and *Culex*. In Polynesia, the principal vectors are *Aedes* spp. and main breeding habitats are small freshwater collections such as leaf axils, tree holes, crab holes, coconut shells, cans, bottles, etc. *Anopheles* spp. are the principal vectors in Africa, Papua New Guinea and some parts of South Asia (where these mosquitoes are also vectors of malaria). Although *Anopheles*

spp. generally breed in clean rural freshwater bodies, some species have adapted to breeding in peri-urban and sometimes even in more central urban areas, where they propagate in sufficient numbers to transmit urban malaria. However, their role in transmission of *W. bancrofti* in urban areas has not been thoroughly investigated. *Culex* spp. are the vectors in large parts of Asia, Central and South America and East Africa and are probably responsible for more than half of all transmission of *W. bancrofti*. In particular *Culex quinquefasciatus* is a widespread vector. As it can breed in water with a high content of organic matter (including latrines), it is often found in high densities in urban environments, in particular in areas with poor drainage and sewerage facilities. This species has been responsible for almost all documented transmission of urban LF so far.

LF infections have traditionally been diagnosed by detection and identification of mf in blood specimens (mainly stained blood smears). New and more sensitive diagnostic techniques have been developed based on detection of specific circulating filarial antigens (CFA) released by the adult worms (for *W. bancrofti* in humans), by specific antibody based tests (for *B. malayi* in humans), or by PCR detection of parasite DNA (for all three species; in both humans and vectors). Clinical disease primarily results from damage caused by the adult worms in the lymphatic vessels. The common clinical manifestations (e.g. acute filarial fever, lymphoedema, elephantiasis and hydrocele) can incur considerable incapacity to the affected individuals, with consequent loss of income and social and psychological stress, and LF has been recognised a leading cause of long-term disability in the world (Zeldenryk et al. 2011). A large-scale Global Programme to Eliminate Lymphatic Filariasis, coordinated by the World Health Organization, was launched in 2000 (WHO 2010).

Studies on LF in the urban environment

There are no internationally recognised definitions of “urban” and “rural”, and the use of these terms differ markedly from country to country and from one study to the next (Utzinger and Keiser, 2006). For the present review, we include only larger cities with $\geq 50,000$ inhabitants as urban, as transmission conditions (especially vector habitats and human behaviour) in smaller human aggregations are considered to be more closely related to those found in rural areas. When reporting on infection in vector mosquitoes, the proportion infected with any stage of filarial larvae is called the “infection rate”, while the proportion with infective larvae is called the “infectivity rate”. Only the later mosquitoes may transmit the infection onwards to new human beings. The terms “annual vector biting rate” and “annual transmission potential” indicate the estimated number of

vector mosquito bites and infective filarial larvae, respectively, a person is exposed to in 1 year. The main findings from documented studies on urban LF carried out since 1950 are summarised below and in Table 1. All the studies have dealt with *W. bancrofti* infections.

Indonesia

Two series of comprehensive studies on LF were carried out in Jakarta, Indonesia, during 1956–1960 and 1974–1975, respectively. The first was in a crowded traditional residential area which had no electricity or running water (Joe et al. 1958, 1960; Chow et al. 1959). It had “unhealthy” sanitary conditions, and the population comprised of labourers, small vendors, drivers, servants and small-scale farmers from the lower socio-economic class. Blood smears from about 7,000 individuals (all ages) were examined, and 7.8 % were mf-positive. The prevalence rose to 10.4 % when people who had lived in the area for less than 3 years were excluded, suggesting local transmission. Clinical examinations in one section of the area revealed no elephantiasis, but hydrocele was noted in 15.2 % of adult males. Dissection of almost 25,000 *C. quinquefasciatus* collected during a 1-year period showed an infection rate of 1.8 % and infectivity rate of 0.3 %. Main breeding places were ditches and pools with polluted water. In a more rural part of the same district, examination of 196 individuals gave an mf prevalence of 16.3 % (19.4 % among those born in the area) and dissection of more than 17,000 *C. quinquefasciatus* gave infection and infectivity rates of 3.5 and 0.1 %, respectively. Waste water pools, present near every well, were the main breeding places.

The other series of studies took place in a crowded slum area with open drains in which *C. quinquefasciatus* bred prolifically (Oemijati et al. 1975; Mahfudin et al. 1977; Self et al. 1978). A small initial survey based on membrane filtration of venous blood showed an mf prevalence of 31.2 % among individuals aged 5 years and above. An area located along a small road (with a clogged open sewage system carrying high populations of *C. quinquefasciatus*) underwent more detailed investigations. Blood smear examination indicated an mf prevalence of 4.5 %, and clinical examination that 2.7 % had signs of LF (hydrocele and lymphoedema). When houses were divided in two groups based on quality of construction, individuals living in poor houses had nine times higher mf prevalence and five times higher disease prevalence than those living in good houses. The population turnover was high (24 % in 2 years), and the prevalence of mf and clinical manifestations increased with duration of residence in the area. More than 99 % of mosquitoes collected during a 1-year period were *C. quinquefasciatus*, with 1.6 % infected and 0.4 % infective. It was estimated that on a yearly basis, a person would on average be bitten 223,000 times and exposed to 1,941 infective larvae of *W. bancrofti*.

Burma

The WHO Filariasis Unit carried out detailed studies on the biology and control of *C. quinquefasciatus* in Rangoon in the 1960s (Williams 1968; Abdulcader 1971). The city had prolific breeding of this vector, mainly in uncovered clogged surface drains. Studies on the transmission of *W. bancrofti* in a densely populated one-square-mile area are of particular interest to the present review (De Meillon et al. 1967; Hairston and De Meillon 1968; Lindquist et al. 1967). Screening of more than 11,000 individuals (all ages) showed an mf prevalence of 4.9 %. Catching of mosquitoes during a 1-year period indicated a mean *C. quinquefasciatus* biting rate of 227 per person per day, giving a total rate of almost 83,000 bites per year. Upon dissection, 0.36 % of the vectors contained infective larvae, resulting in an average exposure to about 300 infective bites per person per year. By combined analysis of the human age–prevalence curve for mf and the infectivity rate for the vectors, it was estimated that about 15,500 bites by infective mosquitoes were necessary to produce one case of microfilaraemia in the human population.

India

Studies carried out during 1966–1971 documented LF infection, disease and transmission in a suburb of Calcutta (Rozeboom et al. 1968; Bhattacharya and Gubler 1973; Gubler and Bhattacharya 1974; Dondero et al. 1976). The area was characterised as congested with poor sanitary facilities and drainage ditches with prolific breeding of *C. quinquefasciatus*. There was a high population turnover (21 % in 1 year), mostly due to males migrating for work but also due to individuals moving between the suburb and familial home villages. Blood surveys indicated an mf prevalence of about 15 %. Only little lymphoedema was seen, but 54 % of adult males had hydrocele. Vector studies indicated a very high biting rate (115,000 bites per person per year) and annual transmission potential (5,904). A smaller side-study compared the situation in the suburb to that of a more central part of the city with multi-storeyed dwellings with indoor toilets and underground drains. Mf prevalence, vector biting density and transmission intensity were all much higher in the suburb. A later study (Hati et al. 1989) compared the prevalence of mf and filarial disease, and the vector biting rate and transmission potential in central Calcutta to that in a rural village located about 80 km away and concluded that all these indices were higher in the urban than the rural area.

The city of Pondicherry in south-eastern India has been a focus for studies on LF since the mid-1970s (Rajagopalan et al. 1977) when blood surveys among all age groups from 14 localities showed an mf prevalence range of 10.2–30.0 %

Table 1 Overview of major studies on urban LF. For all listed studies, the vector was *C. quinquefasciatus* and the parasite was *W. bancrofti*

City (country)	Location (number of urban sites examined)	Human mf prevalence in blood smears, range (mean)	Annual vector biting rate ^a	Vector infectivity rate ^b	Annual transmission potential ^c	Key references
Jakarta (Indonesia)	Rawasari District (2)	7.8–16.3 %	–	0.1–0.3 %	–	Joe et al. 1958, 1960; Chow et al. 1959
	Kepu District (1)	4.5–8.8 %	223,000	0.3–0.4 %	1,941	Oemijati et al. 1975; Mahfudin et al. 1977; Self et al. 1978
Rangoon (Burma)	Kemmendine	4.9 %	83,000	0.36 %	1,357	De Meillon et al. 1967; Hairston and De Meillon 1968
Calcutta (India)	Howrah suburb (1)	12.4–14.8 %	115,000	1.5 %	5,904	Bhattacharya and Gubler 1973; Gubler and Bhattacharya 1974; Dondero et al. 1976
	Central Calcutta (1)	2.5 %	55,000	0.3 %	319	Hati et al. 1989
Pondicherry (India)	Pondicherry City (14)	10.2–30.0 % (17.8 %)	88,500	1.25 %	5,178	Rajagopalan et al. 1977
	Pondicherry City (1)	8.4 %	26,200	0.86 %	450	Rajagopalan et al. 1987, 1989; Ramaiah et al. 1992
Chennai (India)	Chennai City (7)	1.1–7.3 %	–	–	–	Hyma et al. 1989
	Chennai City	0.0–4.5 %	–	–	–	Ramaiah et al. 2005; Kumar and Ramaiah 2008
Greater Recife (Brazil)	Recife City (2)	9.3–10.7 %	–	–	–	Albuquerque et al. 1995a and b; Braga et al. 1998
	Recife and Olinda cities (2)	12.3–13.5 %	–	–	–	Maciel et al. 1994
Maceio (Brazil)	Recife City (31)	0.0–14.6 % (6.5 %)	–	–	–	Maciel et al. 1996
	Jaboatão dos Guararapes (12)	0.0–5.2 % (2.2 %)	–	–	–	Bonfim et al. 2003
Maceio (Brazil)	Jaboatão dos Guararapes (7)	0.0–2.9 % (0.8 %)	–	–	–	Medeiros et al. 2008
	Jaboatão dos Guararapes (25)	0.0–5.1 % (1.4 %)	–	–	–	Bonfim et al. 2009a, 2009b, 2011
Maceio (Brazil)	Maceio City (33)	0.0–5.3 % (0.7 %)	–	0.0–2.1 %	–	Fontes et al. 1994, 1998
	Maceio City (4)	0.0–5.4 % (2.1 %)	–	–	–	Rocha et al. 2000

^a Estimated no. of mosquitoes biting one person in 1 year^b Percent of vectors with infective larvae^c Estimated no. of infective larvae to which one person is exposed in 1 year

(mean 17.8 %). Elephantiasis of the leg was observed in 1.9 %. Intense breeding of *C. quinquefasciatus* was noted in open drains, polluted rainwater pits and accumulations of waste water around houses. Entomological surveys indicated an average vector biting rate of 242 per person per night (about 88,500 per year) and a vector infectivity rate of 1.25 %. It was estimated that a person received an average of 1,106 infective bites and was exposed to 5,178 infective larvae in a year. Laboratory studies indicated that *C. quinquefasciatus* was an inefficient vector because of its short life span, and it was concluded that transmission only took place because the inefficiency was compensated for by the very high vector density.

Pre-control surveys for mf and transmission were carried out in Pondicherry during 1979–1981 (Rajagopalan et al. 1987, 1989; Ramaiah et al. 1992). Almost 25,000 individuals were examined, and 8.4 % were mf-positive. Profound breeding of *C. quinquefasciatus* was again reported, and studies indicated a biting rate of more than 26,000 per person per year and an annual transmission potential of 450. A later interview-based study (Snehalatha et al. 2003) showed that a high proportion of inhabitants considered the biting nuisance around households to be severe and used various measures for protection (mainly mosquito coils, vaporising mats and electric fans). This use, and the expenditures incurred, was higher in the urban than in rural areas. Knowledge about the role of mosquitoes in disease transmission was also higher in urban than in rural areas. Another interview-based study among patients with LF disease in Pondicherry and in two nearby cities (Nanda and Krishnamoorthy 2003) showed that more patients undertook treatment, and that treatment was considerably more expensive in the urban areas compared to what had been seen in previous similar studies in rural areas.

Hyma et al. (1989) reported data from 1974–1986 from LF clinics in the city of Madras (Chennai), Southern India, which indicated that infection and disease occurred to varying extents throughout the city. According to Ramaiah et al. (2005), Chennai has a vast network of poorly maintained sewage canals which are important breeding sites for *C. quinquefasciatus*. Interview-based surveys in different sections of the city (Ramaiah et al. 2005; Kumar and Ramaiah, 2008) indicated that knowledge about LF was higher in high- than in low-income sections, whereas clinical LF was more common in low- than in high-income sections. Many more individuals from low- than high-income sections indicated that they would accept to consume tablets in a mass drug administration programme. The use of personal protection measures was generally high in all income sections, but the type of measures varied between the sections, mainly because of different costs. Spot checks for microfilaraemia in the surveyed city sections indicated that the mf prevalence decreased with increasing income level.

Brazil

The LF situation in Brazil is different from that of most other endemic countries in that transmission is almost exclusively urban. Apparently LF was brought to Brazil with slaves from Africa, and the parasite was transmitted in the new environments by already established urban *C. quinquefasciatus*.

The city of Recife has the most important endemic focus in Brazil. A survey among 4,600 individuals (5–65 years) in two slum areas during 1990–1991 showed mf prevalence rates of 9.3 and 10.7 % (Albuquerque et al. 1995a, b; Braga et al. 1998). The overall LF disease prevalence was 6.3 % (mainly hydrocele and lymphoedema). The risk of being mf-positive was greater among those who had lived in the area for more than 5 years, and among those not using bed nets. Children (5–14 years) had significantly higher risk of being mf-positive if they lived in households with an mf-positive adult. A city-wide survey covering 10,600 individuals (5–65 years) from 31 sites during 1991–1992 (Maciel et al. 1996) showed mf prevalence rates between 0.0 and 14.6 % (overall mean 6.5 %). Large numbers of *C. quinquefasciatus* were collected inside houses. Many areas in the city had no sewerage and drainage facilities, and rapid rural–urban migration and unplanned urbanisation had led to an increase in stagnant surface waters which contributed to the successful breeding of the vectors.

Nearby cities within the greater metropolitan Recife area also have foci of LF, especially Olinda and Jaboatão dos Guararapes (Medeiros et al. 1999, 2008). A study in 1991 (Maciel et al. 1994) compared LF in two slum areas of Recife City to two in Olinda and found overall mf prevalence rates of 13.5 and 12.3 %, respectively. A survey in 2002 among 9,520 individuals (all ages) in Jaboatão dos Guararapes (Bonfim et al. 2003) showed an mf prevalence of 2.2 % (range 0.0–5.2 % in 12 neighbourhoods). Another survey in 2002 among 4,365 individuals (all ages) showed 0.8 % mf prevalence (range 0.0–2.9 % in 7 neighbourhoods), and 2.0 % of examined males had hydrocele (Medeiros et al. 2008). The highest mf prevalence was found in the neighbourhood that also had the poorest sanitary conditions. A large survey during 2000–2002 covering 24,700 individuals (all ages) from Jaboatão dos Guararapes (25 districts; 484 census tracts) showed an overall mf prevalence of 1.4 % (Bonfim et al. 2009a, b). Twenty-eight percent of census tracts had one or more cases of mf (with highest prevalence being 25 %), and a positive association was found between mf prevalence and an established Socio-environmental Composite Risk Indicator for census tracts (Bonfim et al. 2009a). Eighty percent of the districts had one or more positive cases of mf (with highest prevalence of 5.1 %), and a positive association was observed between mf prevalence and an established Social Deprivation Index for districts (Bonfim et al. 2009b). The authors concluded these studies by utilising the established indicators/indices

for spatial analysis and risk-mapping of LF in the urban environment (Bonfim et al. 2011; Brandão et al. 2011; Medeiros et al., 2012).

LF was highly prevalent in the city of Maceió in the early twentieth century, but measures applied by the national LF control programme reduced it to presumed extinction. Reports of locally acquired cases around 1990 therefore triggered a large survey (Fontes et al. 1994, 1998), during which more than 10,000 pupils attending evening classes (aged 10–56 years) were examined for mf. Findings indicated a focal distribution, with 84 % of cases originating from three of the city's 33 neighbourhoods (5.3, 3.5 and 1.2 % prevalence, respectively) characterised by having polluted stagnant water around houses and high population density. Most other mf-positive pupils lived in neighbourhoods close to these, and most of the mf-positives were born and raised in Maceió. *C. quinquefasciatus* from the neighbourhood with highest mf prevalence had infection and infectivity rates of 4.6 and 2.1 %, respectively. Later state-wide mf surveys only detected mf-positive cases in Maceió and confirmed the high prevalence in the already identified endemic neighbourhoods of this city (Rocha et al. 2000). Following implementation of control measures, the mf prevalence in Maceió decreased and examination of almost 23,000 evening students and school employees in 2006/2007 identified only one case of mf (Leite et al. 2009).

The city of Belem in the Amazon region was once one of the most endemic LF foci in Brazil. A survey in 1952 gave an mf prevalence of 19.9 %, which was mainly ascribed to an extraordinary high density of *C. quinquefasciatus* (Neto 1993). Effective control campaigns (diethylcarbamazine treatment and vector control), probably combined with increased living standards, resulted in a steep decrease in prevalence during the following years. Examination of 92,000 people in 2002 and 72,000 in 2003 showed no mf-positive cases and dissection of 25,000 *C. quinquefasciatus* during these 2 years showed no vector infection (Fontes et al. 2005), indicating that transmission in this focus had been or was close to be interrupted.

Sub-Saharan Africa

In sub-Saharan Africa, *W. bancrofti* is mainly transmitted by *Anopheles* spp. Many larger cities apply measures against these vectors for control of malaria, and the vectors are therefore usually not found in large numbers, at least in the more central parts of the cities. *C. quinquefasciatus* is increasingly becoming important as a vector of LF in eastern Africa, especially in urban and semi-urban settings. However, little is known about the extent of urban LF transmission in sub-Saharan Africa.

Two small studies assessed the potential for urban transmission of LF in West Africa. One was in the cities of Bakwu, Bolgatanga and Secondi/Takoradi in Ghana (Gbakima et al.

2005). The survey sites were slum areas with abundant mosquito breeding. Elephantiasis of the leg and cases of CFA positivity were observed in the two later cities. Dissection of *Anopheles gambiae* and *C. quinquefasciatus* did not reveal filarial infections, but analysis of pools of mosquitoes by PCR gave a positive response with *A. gambiae* pools from Bolgatanga. In another study, adults attending clinics in the city of Jos, Nigeria, were examined for LF during a 1-month period (Terranella et al. 2006). The clinics were located in slum areas close to mosquito breeding sites. Among 30 suspected cases of clinical LF, 18 had lived in Jos for more than 5 years, and among 98 CFA tested individuals, six were positive and had lived in Jos for more than 5 years. The majority of these cases came from two urban neighbourhoods, thus suggesting a focal transmission.

Few details are available on urban LF in East Africa. A small survey in Mombasa, Kenya, indicated a low prevalence of mf (2.6 %) despite a large number of *C. quinquefasciatus* vectors (Nelson et al. 1962). Much higher mf prevalence rates (15–25 %) were reported from adults in Dar es Salaam, Tanzania (Minjas and Kihamia 1991), and open drains were identified as important breeding habitats for the potential *Anopheles* sp. and *C. quinquefasciatus* vectors of LF in Dar es Salaam (Castro et al. 2010). A pre-control mf prevalence of 12 % was reported from the city of Zanzibar (range of 9–16 % in different locations), where the *C. quinquefasciatus* vectors mainly multiplied in pit latrines and cesspits but also in flooded basements of apartment blocks (Maxwell et al. 1999).

Epidemiological characteristics of urban LF

Vectors

A major characteristic of the study sites referred to above was abundant proliferation of *C. quinquefasciatus* mosquitoes in local polluted water bodies. Evidently, these vectors were the key culprits responsible for the urban LF transmission. Unplanned urban areas with poor sanitary, draining and sewerage facilities provide favourable conditions and often support enormous breeding of this species, leading to extremely high biting rates. The tendency of such conditions to be concentrated within certain localities of the cities (usually occupied by the less privileged segment of the urban population), combined with a limited vector flight range, leads to another major characteristic of urban LF, namely a marked focality. Interestingly, several of the studies reported that the urban *C. quinquefasciatus* were short-lived, with full development of filarial larvae only taking place in a few longer-than-average living specimens, and that the maintenance of LF transmission by this vector appeared to be possible only because of an extraordinary high density (Joe et al. 1960; Rozeboom et al. 1968; Rajagopalan et al. 1977; Kumar and Ramaiah 2008).

The role of *Anopheles* and *Aedes* mosquitoes in transmission of urban LF, in geographical regions where these genera predominate as vectors, is less clear. It is likely that intervention measures applied against *Anopheles* and *Aedes* in many larger cities (to protect inhabitants from malaria and arbovirus infection) reduce their density to levels below which LF transmission can occur. This, combined with their requirement for relatively clean water for breeding, suggest that their potential as urban LF vectors will be greatest in small- to medium-sized cities, as in the case of Bolgatanga in Ghana, where PCR analysis of *A. gambiae* gave a positive response for *W. bancrofti* (Gbakima et al. 2005).

Infection and disease burden

In some of the surveyed urban sites, the prevalence of *W. bancrofti* infection was low. However, mf prevalence rates above 10 % were reported from several sites that also had high transmission rates (Joe et al. 1960; Bhattacharya and Gubler, 1973; Oemijati et al. 1975; Rajagopalan et al. 1977; Maciel et al. 1994; Albuquerque et al. 1995b) (Table 1). In this respect, it is noteworthy that screening methods and approaches in the different surveys often differed in sensitivity, thus making it difficult to compare findings from one survey to another. The age of the surveyed population (especially whether or not children were included) moreover affected the prevalence.

From some urban sites, clinical manifestations were reported to be rare (Joe et al. 1958; Dondero et al. 1976), but whether the disease prevalence in general differed from that of rural areas with the same level of exposure was unclear. Various factors which differ between urban and rural communities may influence disease prevalence. In some regions, severely diseased urban individuals tend to return to their native rural village (Gubler and Bhattacharya 1974), whereas in other regions, migration may be in the opposite direction due to stigmatisation of severely affected individuals in the village. In respect to elephantiasis, the urban population is less exposed to injuries of the feet and lower legs than rural

populations, and therefore less likely to contract the bacterial and fungal co-infections considered important for the development of this condition. In some surveys, males were moreover not physically examined for hydrocele (only asked if they were affected), and in others, they were reluctant to have their genitals examined (Mahfudin et al. 1977). Overall, however, there was no clear indication of major differences in pattern of infection and disease prevalence between the surveyed urban sites and that reported from rural areas.

Characteristics of major epidemiological determinants

Table 2 gives an overview of major epidemiological determinants and their characteristics as seen in the summarised studies on urban LF. The general picture was that of areas with poor environmental infrastructure, high population density and turnover, low income and educational level, and low social coherency. As outlined, each of these characteristics support transmission and/or oppose its prevention in its own specific way. The characteristics are moreover closely interlinked and in essence related to the prevailing socio-economic conditions.

The most consistently reported characteristic among these determinants was a poorly developed environmental infrastructure, in particular in relation to water drainage, leading to stagnant water collections around or near houses which supported prolific breeding of *C. quinquefasciatus*. Lack of sewerage system (Neto 1993; Rajagopalan et al. 1977; Albuquerque et al. 1995a, b; Maciel et al. 1996; Fontes et al. 1998) and poorly maintained (damaged and/or clogged) open drainage systems (Oemijati et al. 1975; Mahfudin et al. 1977; Self et al. 1978; Williams 1968; Abdalcader 1971; Rozeboom et al. 1968; Rajagopalan et al. 1977; Albuquerque et al. 1995b) were some of the most commonly reported causes for creation of highly productive vector breeding sites. Others were waste water pools near houses and wells (Chow et al. 1959; Joe et al. 1960; Gubler and Bhattacharya 1974; Rajagopalan et al. 1977), urban swamps and ponds (Williams

Table 2 Overview of major epidemiological determinants and their characteristics in areas with documented transmission of urban LF

Major determinant	General characteristics	Implications for LF transmission
Environment	Poor sewerage, drainage and sanitary facilities	Creation of favourable conditions for breeding of vectors, especially <i>C. quinquefasciatus</i>
Demography	High population density and migration rate	Human crowding favours transmission. Influx of new infections from rural to urban areas
Economy	Poorer segment of population (lower socio-economic class)	Poor quality of houses with little or no mosquito proofing. Personal protection measures against mosquito bites can be unaffordable
Knowledge	Low educational level and knowledge about LF	Little understanding of disease transmission. Importance of preventive/protective/control measures not clearly envisaged
Behaviour	Mixed cultures, low social coherency. Privacy and individualism given high value	Reluctance towards diagnostic and clinical surveys, and opposition to participate in mass treatment campaigns

1968; Rajagopalan et al. 1977, 1987), urban agriculture (Joe et al. 1958), wet pit latrines (Williams 1968; Maxwell et al. 1999) and even flooded basements (Maxwell et al. 1999).

In terms of demographical features, the LF endemic urban areas were generally densely populated (Lindquist et al. 1967; Rozeboom et al. 1968; Gubler and Bhattacharya 1974; Fontes et al. 1998). Crowding is well known to favour transmission of infectious diseases, and in consistence with this, it was noted in Recife that the risk of being mf-positive was directly related to the number of individuals in the household (Braga et al. 1998). The LF endemic urban foci frequently also had a high population turnover, with influx of new inhabitants from endemic rural areas that could potentially carry new infections from rural to urban areas (Self et al. 1978; Gubler and Bhattacharya 1974; Mahfudin et al. 1977; Rajagopalan et al. 1987). However, that this was not the primary source of urban infections was supported by the finding in some of the studies of higher mf prevalence among long-term residents than among those who had recently arrived (Joe et al. 1958, 1960; Self et al. 1978; Albuquerque et al. 1995b).

When considering economical capability, it was obvious that urban LF was most prevalent in areas inhabited by the low-income segment of the population. For example, spot checks in different parts of Chennai indicated that the mf prevalence increased with decreasing income level (Kumar and Ramaiah 2008), and analysis of a large data set from Jaboatão dos Guararapes showed a positive association between mf prevalence and worsening socio-economic conditions (Bonfim et al. 2009a, 2009b). In several of the other studies it was similarly noted that the poorer city parts were most affected whereas richer parts were less or unaffected (Joe et al. 1958; Bhattacharya and Gubler 1973; Albuquerque et al. 1995b; Fontes et al. 1998). In addition to affect peoples' ability to afford personal protective measures against mosquitoes and medicines for the treatment of LF (Snehalatha et al. 2003; Ramaiah et al. 2005), their economy plays a major role for the quality of housing they can afford. This includes the type of water and sewerage facilities and the extent to which houses are proofed against mosquito entries. Even within a highly endemic area of Jakarta, it was observed that the quality of individual houses had a marked effect on the risk of LF infection (Mahfudin et al. 1977). With urban LF mainly being transmitted in low-income areas, it might be expected that the educational level and knowledge about LF is often poor in the affected population. Although rarely addressed in the studies, this general assumption was supported by surveys in Chennai showing that knowledge about the cause of the clinical manifestations of LF and about the role of mosquitoes in LF transmission was closely related to household income (Ramaiah et al. 2005; Kumar and Ramaiah 2008). The importance of preventive and control measures may therefore often not be clearly envisaged by those most affected.

Human behaviour and culture often differ markedly between rural and urban communities. Many urban areas are characterised by mixed cultures and low social coherency, and privacy and individualism are given high value. Urban populations are generally busy with their daily activities and their organisation and movements may appear rather chaotic for outsiders. These characteristics may not have major effects on LF transmission but certainly can have on efforts to survey, manage and control LF in the urban environment. More often than for rural populations, urban populations prefer individual consultation and treatment in clinics, for which they may be willing to incur high expenditures (Snehalatha et al. 2003), and there may be reluctance to participate in communal activities such as disease surveys (Mahfudin et al. 1977) and treatment campaigns (Ramaiah et al. 2005; Addiss 2010). Pre-control surveys in Chennai indicated that much fewer individuals from high- than low-income urban areas would accept to consume tablets during a mass drug administration (MDA) programme, and that drugs would only be accepted if delivered by official health service personnel and not by local people (Ramaiah et al. 2005). Strategies for control of urban LF need to adapt to these behavioural characteristics. In this respect, it may be considered to focus MDA on identified high-risk areas and to pay increased attention to health information messages, personal vector protection measures, improvement of environmental infrastructure and general vector control.

Conclusion

Studies on urban LF and the environmental, socio-economic and behavioural basis for its occurrence are relatively few and, for many of them, rather old. Most have been carried out in large megacities, whereas, only few have addressed the small- and medium-sized cities which now have the highest potential for growth. With the current tremendous increase in urban populations, and the increased focus on worldwide LF elimination, there is a need for more studies which can provide a strong knowledge base for design of programmes specifically addressing control of LF in the urban environment.

Key issues for future research include (1) the potential of *Anopheles* sp. and *Aedes* sp. for transmission of urban LF, (2) the socio-economic and human behavioural context of urban LF, (3) the epidemiology of LF in small- to medium-sized cities, (4) methods for rapid identification and mapping of urban risk areas (e.g. based on *Culex* breeding or socio-economic index), (5) how to most effectively increase people's perception and understanding of LF in affected urban areas and how best to mobilise them for participation in control activities and (6) the effect of climate change on urban transmission of LF. There is also a need for gathering and analysing experience from more recent but still undocumented

attempts to control LF in urban environments (also in cases where these have failed). Various measures for control are available but experience with these primarily stem from rural areas. As seen from the present review, environments, socio-economic conditions and human behaviour differ markedly between rural and urban areas and even within different sections of urban areas. These differences have important effects on the epidemiology of LF and should be taken into consideration when selecting measures and designing strategies for successful control of LF in the urban environment.

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