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Situation of Sri Lanka, where autochthonous malaria is no longer a problem, and other infections dominate, such as dengue, leptospirosis and rickettsioses

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Purpose of review
Sri Lanka achieved a major milestone in communicable disease control in 2012 by reporting zero incidence of autochthonous malaria. However, reduction of malaria was associated with concurrent increase of several tropical diseases. This review looks into the time trends and epidemiology of these communicable diseases in Sri Lanka.

Recent findings
Reduction of malaria cases coincides with an increase of dengue, leptospirosis and rickettsioses in Sri Lanka. Although the case fatality rate of dengue has reduced and maintained below 1%, leptospirosis in clinical management is questionable. Despite having national focal points for control and prevention, these emerging diseases are completely out of control. Whether the holding back of vector control activities of malaria after a successful control programme is having an effect on emergence of other vector-borne diseases should be studied.

Summary
The communicable disease control programme in Sri Lanka should be further strengthened with availability of proper and rapid diagnostic facilities. Malaria control could not be considered as a great achievement due to the fact that other emerging infectious diseases are replacing malaria.

Keywords
dengue, leptospirosis, malaria, rickettsioses, Sri Lanka

INTRODUCTION

The national malaria control programme of Sri Lanka declared zero incidences of autochthones malaria cases in 2012. Since then, the indigenous transmission of malaria was not reported in Sri Lanka. However, imported cases continued to report due to international travel and trade. Sri Lanka has achieved malaria elimination goals approximately 2 years prior to its targeted deadline. Malaria was once considered the biggest public health threat in this island nation. Control of one of the deadliest and globally widespread communicable diseases in Sri Lanka seemed an important milestone in Sri Lankan communicable disease control programme. Nevertheless, epidemics of emerging and re-emerging communicable diseases such as dengue, leptospirosis and Rickettsial infections coincides with control of malaria in Sri Lanka, and at present, these diseases are considered as leading public health threats. This study discusses the control of malaria and emergence of new infectious diseases in Sri Lanka.

MALARIA IN SRI LANKA

Malaria was reported in Sri Lanka since early civilization and some historians believe that malaria could be a reason for the change of old kingdoms from the dry zone of the country to the wet zone. In Sinhalese literature, malaria was reported as '*Kala*

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KEY POINTS

- Indigenous transmission of malaria is eliminated in Sri Lanka and the last case was reported in 2012.
- Dengue, leptospirosis and other infectious diseases such as rickettsioses emerged as new threats in Sri Lanka.
- Public health strategies, which were successful in malaria elimination, failed to control emerging infectious diseases.

Una' and commonly reported as a cause of death in dry zones of Sri Lanka. The largest well documented outbreak of malaria in Sri Lanka was reported in the 1934–1935 period with more than 70 000 deaths attributed to the malaria epidemic within a 6-month period, nearly 1.3% of the total population. During the peak of the outbreak, 60 000 outpatient attendances per day were reported due to fever [1,2]. After the massive impact of this outbreak, the malaria control programme was strengthened with the support of both public and government. As a part of the malaria control programme in Sri Lanka, dichlorodiphenyl-trichloroethane (DDT) spraying was launched in 1945 [3]. After the 1955 world health assembly, malaria eradication goals were adopted in Sri Lanka with the establishment of the Anti-Malaria Campaign in 1958 [4]. The considerable drop of malaria cases after 1945 was mainly attributed to indoor residual spraying of DDT, and this trend continued steadily. In 1963, the total number of malaria cases reported was 17 with only six indigenous cases [5]. Sri Lanka almost celebrated malaria elimination in that year and routine DDT spraying was discontinued, and it was limited to barrier spraying around forests. Resurgence of malaria within months of cessation of vector control activities in Sri Lanka is globally considered as an important lesson learnt on malaria control. This setback of malaria control led to a sustained outbreak of malaria in Sri Lanka with over half a million cases by 1967. Sri Lanka was once again considered as a malaria high endemic country after 1967. Malathion was introduced as the main measure of mosquito control in 1977 after emergence of DDT resistance [4]. With this introduction, reduction of case numbers was observed for about 3 years and then choloroquine resistant malaria was detected [6]. After 1985, malaria cases steadily increased untill 1987 with more than half a million cases a year. Untill the year 2000, malaria continued to affect Sri Lanka with more than 200 000 cases each year (Fig. 1).

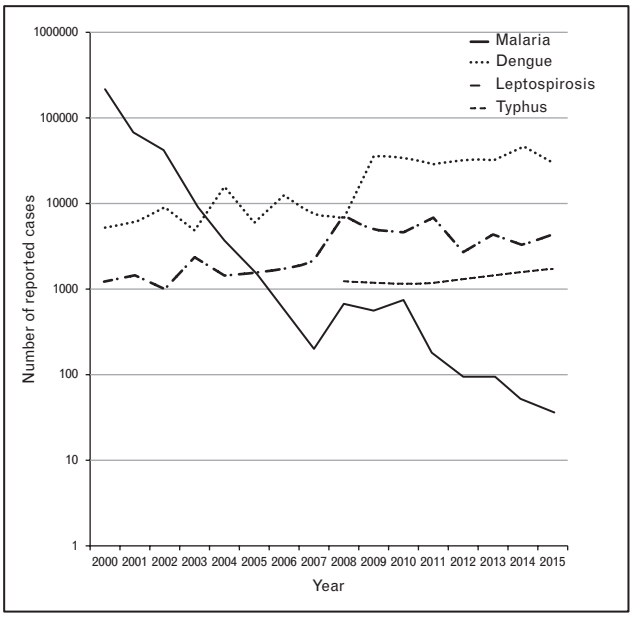

FIGURE 1. Trend of malaria, dengue, leptospirosis and typhus in Sri Lanka (2000–2015).

After the year 2000, a clear and steady decline in annual cases of malaria was observed. In 2006, approximately 50 years after the first near-elimination experience of malaria in Sri Lanka, case numbers dropped to less than 1000. The malaria elimination strategies established in 2008 had clear, outcome-oriented policies with a well-laid implementation plan, which lead to current status of Malaria in Sri Lanka [7,8▪▪]. After the year 2003, only two malaria deaths were reported from Sri Lanka. The last case of malaria due to indigenous transmission was reported in 2012. The total number of imported cases of malaria reported from Sri Lanka was 95, 49 and 36, respectively, for the years 2013, 2014 and 2015.

The final push for malaria elimination in Sri Lanka is a challenge due to several sources of imported cases. The majority of the imported cases are due to deported illegal migrants. In 2012, there were 32 cases of *Plasmodium falciparum* related to human trafficking [9,10]. Screening at the port of entry is used as the key strategy to prevent reintroduction of malaria to Sri Lanka through this route [11]. Sri Lankan armed forces taking part in humanitarian missions in malaria endemic countries is another risk group. However, knowledge as well as adherence to chemoprophylaxis among this group is reported as good [12].

Although malaria is in near elimination state, abundance of vector mosquito will be a major challenge to the last push of malaria elimination. A recent study showed that the primary vector *Anopheles culicifacies* as well as other species of potential

malaria vectors (*A. vagus, A. varuna, A. nigerrimus, A. peditaeniatus* and *A. barbirostris*) were still found to be common in Sri Lanka [13].

DENGUE IN SRI LANKA

In 1962, the first serologically confirmed dengue case was reported in Sri Lanka. Just 3 years after the first detection, an island-wide outbreak of dengue haemorrhagic fever (DHF)/dengue fever occurred in the 1965–1966 period, which mainly involved the Western province [14–16]. There were 51 reported cases and 15 deaths due to dengue fever/DHF from 1965 to 1968 and the predominant etiological agent was dengue virus (DENV) serotype-1 and DENV-2 [15]. Until 1989, DHF was not considered as a major public health issue in Sri Lanka and intermittent cases of all four DENV serotypes were identified while the majority reported from Colombo [16,17]. A large outbreak of DHF with 203 clinically diagnosed cases was observed in 1989 and the epidemic was in and around the Colombo area. The case fatality rate (CFR) was 9.8% [16,18]. In 1996, another outbreak occurred in Sri Lanka with spreading disease to other provinces such as North Western, Southern and Eastern [16]. Children less than 15 years (male predominant) were the main age group affected with peak around 5 years of age [16]. Dengue has a seasonal trend, where two peaks of dengue occur following monsoon rains in the southwestern monsoon (June–July) and the northeastern monsoon (September–December) [16,19]. In 1996, dengue fever/DHF was declared as a notifiable disease in Sri Lanka [20]. In 2002, the island experienced another large outbreak of dengue with 8931 cases and 54 deaths with a CFR of 0.75 followed by another in 2004 with 15 457 cases and 88 deaths [20]. A new distinct clade of DENV-3 was identified during this outbreak [21]. By 2006, dengue started to spread to all other provinces and young adults became an additional risk group [21]. The worst outbreak of dengue was reported in 2009 and 2010 with around 35 000 cases [22]. There were concurrent outbreaks since then and the number of cases were increasing yearly [22]. Conceivably, this increased reporting could also be attributed to the improved awareness and strict disease surveillance. The DENV-1 serotype was predominately isolated recently compared with previous outbreaks and dengue was spreading to other areas of the country including Northern and Eastern provinces [17]. By 2013, dengue fever/DHF cases had been reported from all nine provinces of Sri Lanka including rural areas, while Western province was reporting the largest burden of disease [17].

Both *Aedes aegypti* and *A. albopictus* are demonstrated as main vectors for dengue transmission throughout the country [23,24]. Mosquito breeding places are abundant in Sri Lanka and *Aedes* larvae habitats have been identified even in brackish water in the peri-urban areas of Sri Lanka [25▪]. The main strategy in dengue control is elimination of breeding sites through health promotion and legislative activities. Surveillance, improving management of DHF patients, integrated vector management (vector control and surveillance), strengthening research, emergency response and social mobilization [20,26] are the other main control activities in place. The surveillance system is currently strengthened by establishing web-based surveillance in 50 sentinel hospitals covering all provinces of the country [26]. Despite being clearly prioritized as one of the leading public health issues in Sri Lanka, dengue is still completely out of control and without new strategies dengue will continue to threaten the health of Sri Lankan people.

LEPTOSPIROSIS IN SRI LANKA

In 1959, Rajasuriya *et al.* [27] reported the first confirmed cases of leptospirosis from Colombo. Isolation of *Leptospira* from Sri Lankan patients was first done in 1962 and this isolate was reported as *Leptospira icterohaemorrhagiae* [28]. Once it was established that leptospirosis is common and endemic in Sri Lanka, researchers from different areas of the country reported leptospirosis as a common diagnosis for febrile patients [29]. A serological survey done among probable high-risk groups revealed that the antileptospiral antibodies are common among farmers and animal handlers [30]. Investigations among pregnant women [31] as well as children [32] in Sri Lanka during the 1960–1970 period suggested that many people other than so-called 'high-risk' groups are vulnerable. During the period between 1961 and 1976, around 40 serovars belonging to 20 serogroups of *Leptospira* were isolated from Sri Lanka [33▪▪]. Since 1976, published literatures on leptospirosis in Sri Lanka were scarce until 2006. However, many physicians knew it and the clinical diagnoses of leptospirosis were not uncommon. This disease was declared as a notifiable disease by the Epidemiology unit of Sri Lanka in 1991. Since then, routinely reported data showed around 1500 cases of leptospirosis in each year. In 2003, Sri Lanka experienced a large outbreak of leptospirosis. Investigations into this outbreak revealed that there could be more than one serovar of leptospirosis causing epidemic leptospirosis in Sri Lanka [34]. In 2008, Sri Lanka experienced the largest documented outbreak of leptospirosis with nearly 8000

reported cases [35]. Since 2008, Sri Lanka experienced a sustained outbreak of leptospirosis with an average of 3000–4000 cases each year. Investigations of leptospirosis during the recent past showed that there are at least five species of Leptospira causing human leptospirosis in Sri Lanka [33▪▪]. These include *Leptospira interrogans, Leptospira kirschneri, Leptospira borg-petersenii* and *Leptospira santarosai*. Microgeographical variations of the disease were proposed as an explanation for varied disease severity and manifestations at subnational level [36▪]. Molecular studies on global collection of leptospirosis clearly show that Sri Lankan isolates of *Leptospira* are clearly different from other isolates from the Indian subcontinent [37], showing a genetic deviation a long time ago and evidence to suggest that leptospirosis is not a new disease in Sri Lanka. Multilocus sequence typing of clinical samples from Sri Lanka during the 2008 outbreak suggested that a genotype similar to serovar Lai may be the aetiological agent for the particular outbreak, which was not reported previously [38]. Acute renal failure, myocarditis, pancreatitis, liver failure, heart failure and pulmonary haemorrhages were the commonly reported complications in Sri Lanka.

An outbreak of leptospirosis related to white water rafting in Sri Lanka showed that even white-collar workers could be at risk through water sport [39]. This finding is in par with water sport-related leptospirosis reported worldwide. Host animals for leptospirosis were studied in several recent investigations. In one study, a carrier status of cattle was reported as high as 12.2% [40]. Seroprevalence of antileptospiral antibodies was 38.8% among smallholder dairy cattle. Rodents captured in and around the Kandy area showed a 17.5% seropositivity [41]. Even though several studies evaluated rapid diagnostic tests that are suitable for the Sri Lankan setting [42–44], none of these tests are currently available for routine diagnosis. The major limiting factor for clinical management of leptospirosis in Sri Lanka is considered as the lack of point-of-care diagnostic facilities.

Even though exposure factors were considered as the most important risk factors, using chlorinated water for drinking/general purposes [odds ratio (OR) 0.33], paddy fields in the vicinity of home (OR 1.77), sighting dogs at home yard/dog ownership (OR 1.79), sighting cattle at home yard/cattle ownership (OR 1.69) and history of working in a paddy field (OR 3.02) were the only determinants of leptospirosis confirmed through analytical studies in Sri Lanka [45▪]. Studies on predicting disease severity showed packed cell volume less than 29.8% (OR 3.750), alanine transaminase more than 70 IU/l (OR 2.639) and hyponatremia less than 131 mEq/l (OR 6.413) as risk factors [46]. Oliguria (OR 4.14), jaundice (OR 5.13) and arrhythmias (OR 5.774) were demonstrated as individual risk factors for myocarditis [47]. Mortality among leptospirosis patients was shown to be associated with hyperkalemia [48].

RICKETTSIAL INFECTIONS IN SRI LANKA

Rickettsioses, caused by the obligate intracellular bacteria of the genus *Rickettsia,* are one of the oldest known vector-borne zoonotic infections that represent a diverse clinical spectrum and a significant global morbidity [49]. Different disease patterns of rickettsioses such as spotted fever, typhus and scrub typhus have been defined on the basis of clinical and serological parameters [49]. Incidence of rickettsial infections around the world has been increasing over the last few decades and a comparable tendency is also noticed in Sri Lanka [49–51]. The history of rickettsioses in Sri Lanka runs a long way back towards the early twentieth century with the earliest mention of an epidemic of scrub typhus amongst militants involved in the world war. The first few published reports describe scrub typhus and endemic typhus from different parts of the island including western and central regions, by serological confirmation with Weil Felix test [52]. Since then, only a few studies had focused on rickettsioses in Sri Lanka, and the overall information on the status of rickettsioses in Sri Lanka was scarce until recent work done mainly in Central and Western provinces [53–55].

In the recent past, the country experienced several outbreaks of suspected rickettsial infections and a few key recent studies have confirmed the re-emergence of rickettsioses across the island in a geographically restricted manner [50,53,54,56]. Also, these indicate that the central hills bear predominantly spotted fever (mainly caused by the species *R. conorii*, *R. honei* and *R. japonica*) whereas scrub typhus (caused by *Orientia tsutsugamushi*) and typhus (manly caused by *R. typhi*) are commonly seen in low country wetlands, particularly the western region [53–58]. In addition to Western and Central provinces, the three disease types have been detected in some other parts of the island including Northern and Southern provinces [56,59,60]. As per the national epidemiology unit reports, notification of typhus fever is increasing, denoting a possible rising trend in the spread of the infection, but this needs to be cautiously interpreted, as it could also be due to enhanced interest and awareness about the disease. Jaffna, which represents the northern dry zone of the island, shows an increase in the number of rickettsial cases, scrub typhus in particular, over the last few years [61,62].

Nonspecific clinical manifestations and atypical presentations could hinder the early case detection resulting in fatalities as reported in some studies, and hence needs an early suspicion on rickettsial infections in patients with acute febrile illness with possible complications [55,63▪,64,65]. The infection is reported among a wider age range including both adult and paediatric groups with no significant gender preference [54,56,65]. Mostly, the cases are either from rural or suburban areas in middle or lower socioeconomic classes [50,65]. Also, in addition to the above reported outbreaks, year-round sporadic cases are common with spotted fevers, while scrub typhus seems to have a seasonal preponderance [53]. Occupations involving outdoor activities, including military services, and living around larger vegetations with exposure to wild/domestic animals and arthropod vectors are common local risk factors [53,62,65]. Possible vectors could be the fleas, ticks (typhus and spotted fever) and mites (scrub typhus) in rodents and shrubs [66,67].

DISCUSSION

Malaria control in Sri Lanka was achieved through well planned control and prevention strategies, management guidelines and through a dedicated control programme. Although similar attention is given, primary prevention of dengue is a failure and every year 20–30 000 cases are reported, showing a massive burden to the health system. However, the CFR is now less than 1%, a good indicator of improved clinical management. Although public attention is also given to leptospirosis, a systematic approach in control and prevention is still lacking. As an example, one of the main strategies used for primary prevention is use of doxycycline as a chemoprophylaxis, an intervention that lacks evidence for practice. The available evidence is for postexposure prophylaxis [68] but not for people with continuous exposure and living in an endemic area [69]. Even though Sri Lanka is having the second highest global incidence of leptospirosis, standard diagnostic facilities using a broad panel of serovars are still not available for routine use. Unlike the story of malaria, dengue and leptospirosis, rickettsial infections lack attention towards the discussions on prevention and control so far, possibly with the poor understanding of related factors in the local setting. Although several studies have produced basic details on epidemiology of rickettsioses, none of them have established the exact mode of transmission and the vectors and reservoirs responsible for the rickettsioses in Sri Lanka. Further, the precise diagnosis and identification of specific rickettsial species causing the disease in the local setting is imperative in identifying related risk factors as well as in implementing prevention and control strategies.

Further, the intense malaria control programme, which was primarily through vector control, had an effect of other vector-borne diseases as well. Withdrawal of vector control activities may have led to increase of other vector population triggering the increase of other vector-borne diseases. However, this hypothesis needs to be tested through well planned studies.

CONCLUSION

Despite advances in preventive strategies, antibiotic use and diagnostic facilities, communicable diseases continue to threaten the life of people in Sri Lanka. This is the case in many tropical countries and most of these threats are still not properly identified and prioritized. Dengue has become a global health priority, although some other silent epidemics of infectious diseases such as leptospirosis and rickettsioses threaten the lives of people in these countries, sometimes even more than dengue, due to high CFR. In Sri Lanka, lessons learned from malaria control should be used to control other emerging infectious diseases before these diseases take the place of malaria!

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Conflicts of interest

There are no conflicts of interest.

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