

Review Article

Analysis of Some Societal Factors Constraining COVID-19, Dengue, Malaria and Tick-Borne Borreliosis Control

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Abstract

Some societal factors pose challenges for applying recent scientific discoveries to more effectively control infectious diseases. These limitations are analysed with reference to dengue, malaria, tick-borne borreliosis and COVID-19, in order to promote better understanding and formulate mitigating measures. It is suggested that factors identified for the four diseases may be relevant to other infectious diseases as well

Keywords: *Aedes aegypti*; *Aedes albopictus*; *Anopheles culicifacies*; *Anopheles stephensi*; Borreliosis diagnostics; COVID-19; Dengue; Infectious disease control; Malaria; Media misinformation; Salinity adaptation in mosquito vectors; Societal constraints in infectious disease control; Vaccine hesitancy

Introduction

The benefits conferred by recent scientific discoveries, e.g. new chemotherapeutics, monoclonal antibodies for diagnosis and treatment, recombinant protein antigens for diagnosis, and vaccines for infectious diseases like COVID-19, dengue and malaria, are widely appreciated. However, some societal factors that limit the application of new scientific advances for improving the control of COVID-19, dengue, malaria and tick-borne borreliosis are less well understood. This article separately analyses specific societal constraints in each of these four diseases with the objective of broadening understanding and promoting the development of appropriate measures to mitigate the constraints.

Dengue

Dengue is the most prevalent arboviral disease in the world with 5.2 million annual cases reported to the WHO in 2019, but with a higher estimated global incidence of 100 – 400 million cases [1,2]. Dengue vaccines have recently become available, while anti-viral drugs to specifically treat dengue have yet to be approved [1,2]. *Aedes aegypti* mosquitoes are the principal vectors of dengue and other human arboviral diseases, including chikungunya, yellow fever and Zika, in tropical and sub-tropical countries [1,2]. *Aedes albopictus* is a secondary arboviral vector that has recently expanded its range to several temperate zone countries, partly through developing diapausing eggs able to survive winters [1,2]. Larval source reduction measures are important worldwide for controlling *Aedes* vectors of dengue, in comparison with the spraying of adulticides indoors and the use of insecticide impregnated bed nets which are effective against *Anopheles* mosquito vectors of malaria [1-4]. This is because the two *Aedes* species, in contrast to the *Anopheles* vectors, tend to blood feed on humans outdoors during the day [1-4]. Most countries follow the World Health Organization (WHO) recommendations on vector control [1,3,4] for dengue and other arboviral diseases.

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Development of *Aedes* mosquito vectors in coastal brackish water and implications for the control of dengue and other arboviral diseases

Both *Ae. aegypti* and *Ae. albopictus* are widely regarded to lay eggs and undergo preimaginal development only in fresh water (FW) collections containing $<0.5 \text{ gL}^{-1}$ salt, so that the present WHO [3,4] and US Centres for Disease Control and Prevention (CDC) [2] guidelines for larval source reduction through applying larvicides and eliminating preimaginal habitats are only directed towards their freshwater habitats. The WHO recommends measures to minimize or eliminate freshwater collections where the *Aedes* vectors oviposit and undergo preimaginal development, the application of the organophosphate larvicide Temephos at concentrations up to 1 mgL^{-1} to freshwater storage containers which constitute important *Aedes* larval habitats in the tropics, and space spraying with adulticides during epidemics to control dengue [1,3,4].

Aedes aegypti and *Ae. albopictus*, however, have been reported since 2011 to be capable of ovipositing and undergoing preimaginal development to adulthood in brackish water (BW) habitats of up to 15 gL^{-1} salt in the northern coastal peninsula of Jaffna in the island of Sri Lanka (Figure 1) with FW, BW and saline water being defined as containing < 0.5 , $0.5\text{--}30$ and $> 30 \text{ gL}^{-1}$ salt, respectively [5-10].

The preimaginal development of *Ae. aegypti* and *Ae. albopictus* in BW has since been reported in coastal areas of other countries, including Brunei Darussalam [12], the US [13], Brazil [14], Mexico [15], Indonesia [16], and India [17]. Typical BW habitats of *Ae. aegypti* are BW accumulations in beach debris, fishing boats, and coastal wells, as well as discarded containers in swamps, drainage canals, urban drains, surface ground water and household containers in coastal areas [5-10,12-17]. The variety of BW habitats where *Ae. aegypti* larvae can be found in Jaffna city and other sites in the Jaffna peninsula are illustrated in Figure 2.

BW-derived *Ae. aegypti* and *Ae. albopictus* larvae in the Jaffna peninsula were more salinity-tolerant, possessing higher LC_{50} for salt, than the corresponding FW-derived larvae from the Sri Lankan mainland as shown in Figure 3 [5,10,18]. *Aedes albopictus* was observed to be more salinity tolerant than *Ae. aegypti* at both locations (Figure 3).

Further investigations on laboratory colonies established from field-collected BW and FW *Ae. aegypti* demonstrated that, although they remained reproductively compatible, BW-adapted or salinity-tolerant *Ae. aegypti* significantly differed from FW *Ae. aegypti* in several important biological features summarized in Table 1. These structural and physiological differences are likely to be important for the greater salinity tolerance in BW *Ae. aegypti*.

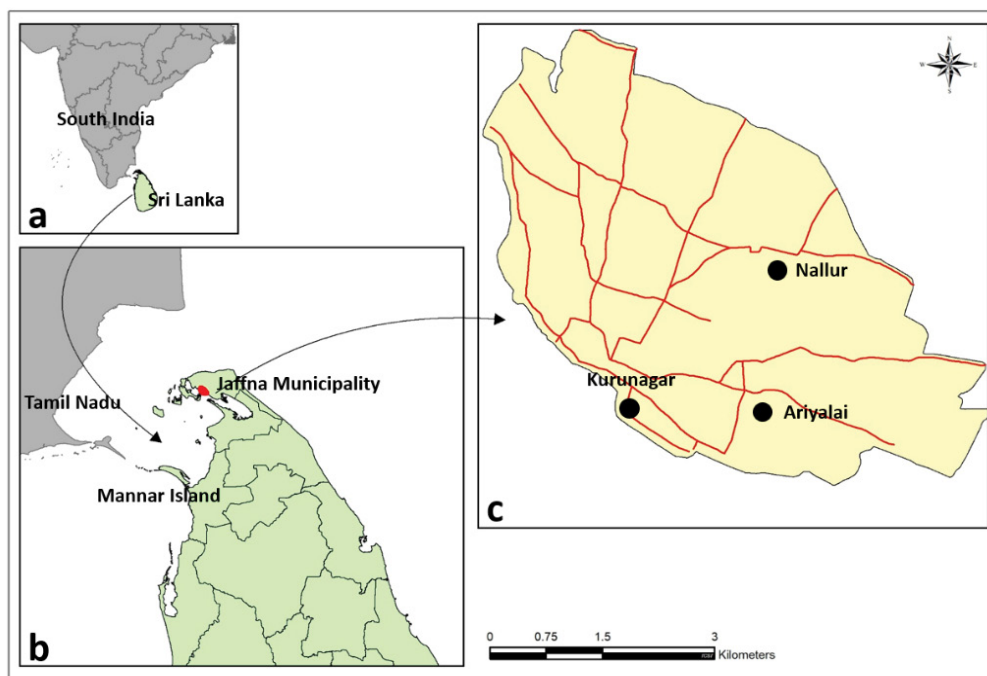


Figure 1: (a) Map showing the location of Sri Lanka in relation to South India; (b) the relative locations of the Jaffna peninsula, Mannar island and Jaffna city within Sri Lanka; (c) sites within Jaffna city where *Anopheles stephensi* (discussed in section on Malaria) larvae are found. Reproduced with permission under the creative commons licence from [11].



Figure 2: BW habitats of *Ae. aegypti* in the Jaffna peninsula, Sri Lanka. Photographs show the brackish water collections containing larvae in: A & B - disused boats; C & E: abandoned wells; D & F: discarded food and beverage containers. Reproduced with permission under the creative commons licence from [5].

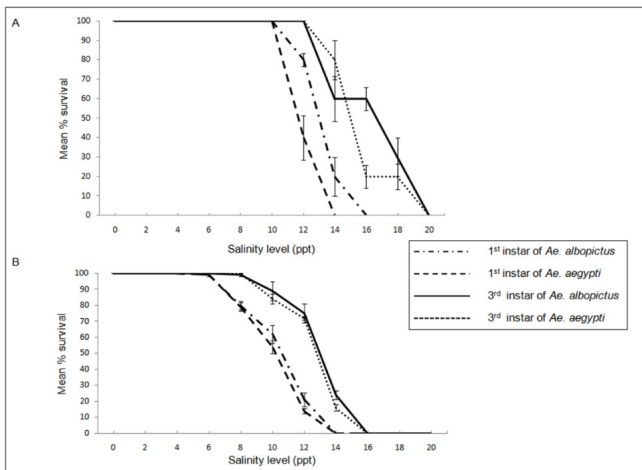


Figure 3: Effect salinity on *Ae. aegypti* and *Ae. albopictus* from (A) coastal Jaffna peninsula and (B) mainland Sri Lanka on the L1 and L3 larvae to adult transformation. L1 and L3 refer to first and third instar larvae respectively. Ppt – parts per thousand or gL^{-1} . Reproduced with permission under the creative commons licence from [5].

It is expected that the salinity-adaptive structural and molecular changes seen in *Ae. aegypti* will be paralleled in the secondary arboviral vector *Ae. albopictus*, as well as other FW mosquito vectors that have adapted to develop in coastal BW, e.g., the malaria vector *Anopheles culicifacies* discussed in section on Malaria. However, further investigations are needed to confirm this hypothesis.

The euryhaline nature of salinity-tolerant *Aedes* vectors in coastal areas and the neglect of BW habitats in vector control programs, allows them to serve as arboviral reservoirs in coastal areas and function as bridging vectors for adjoining inland areas, thereby enhancing arboviral disease transmission and facilitating epidemics as discussed in more detail elsewhere [21]. As a consequence, it may be predicted that small islands and countries with long coastlines in relation to their total

land area, e.g. Indonesia, Sri Lanka and the Caribbean islands, will be particularly prone to the enhanced transmission of arboviral diseases like dengue, chikungunya and Zika [22,23]. Moreover, it is expected that global warming leading to a rise in sea level will increase ground water salinisation in coastal areas, and further exacerbate arboviral disease transmission in this manner [24,25]. Therefore, it is important in coastal zones throughout the world to (i) extend larval source reduction efforts also to the BW habitats of *Aedes* vectors, and (ii) monitor the efficacy of widely-used larvicides such as Temephos in coastal areas because of the demonstrated diminished susceptibility of BW *Aedes* to Temephos [10]. Dengue, the most prevalent arboviral disease world, causes

Table 1: Differences between BW and FW *Ae. aegypti*

Characteristic	Differences	References
LC ₅₀ for salt	Significantly higher LC ₅₀ in BW <i>Ae. aegypti</i> for the L1 and L3 to adult transition which was an inheritable characteristic	[5,10,18]
Osmoregulatory anal papillae in L3 larvae	Significantly larger anal papillae in BW <i>Ae. aegypti</i> which was an inheritable characteristic	[19]
Gene expression in mid-L4 larvae	Marked differences, particularly in genes for cuticle proteins, and others associated with cuticle synthesis	[20]
Protein composition of L4 cuticles	Marked differences compatible with the gene expression data	[20]
Cuticle structure by TEM	Thicker cuticles in L4 larvae and adult abdomen with more prominent endocuticles and exocuticles in BW <i>Ae. aegypti</i>	[20]
Surfaces of shed L3 and L4 cuticles	More pronounced surface undulations in BW <i>Ae. aegypti</i> cuticles by AFM and SEM	[10]
Egg sizes	Significantly smaller eggs in BW <i>Ae. aegypti</i>	[10]
Surfaces of eggs by AFM and SEM	BW <i>Ae. aegypti</i> egg surfaces were significantly less elastic by AFM, with more undulating surfaces seen by AFM and SEM	[10]
Hatchability of eggs and preimaginal development to adults	Hatchability of eggs laid and preimaginal development to adults by FW <i>Ae. aegypti</i> is decreased in 10 gL^{-1} salt BW. These properties were maternally inherited in genetic crosses	[10]
Susceptibility of L3 and L4 to the common larvicide Temephos	BW <i>Ae. Aegypti</i> were significantly more resistant than FW <i>Ae. aegypti</i> in a 24h assay	[10]

L1-L4: first to fourth instar larval stages, AFM: atomic force microscopy, SEM: scanning electron microscopy, TEM: transmission electron microscopy, LC50: concentration producing 50% lethality

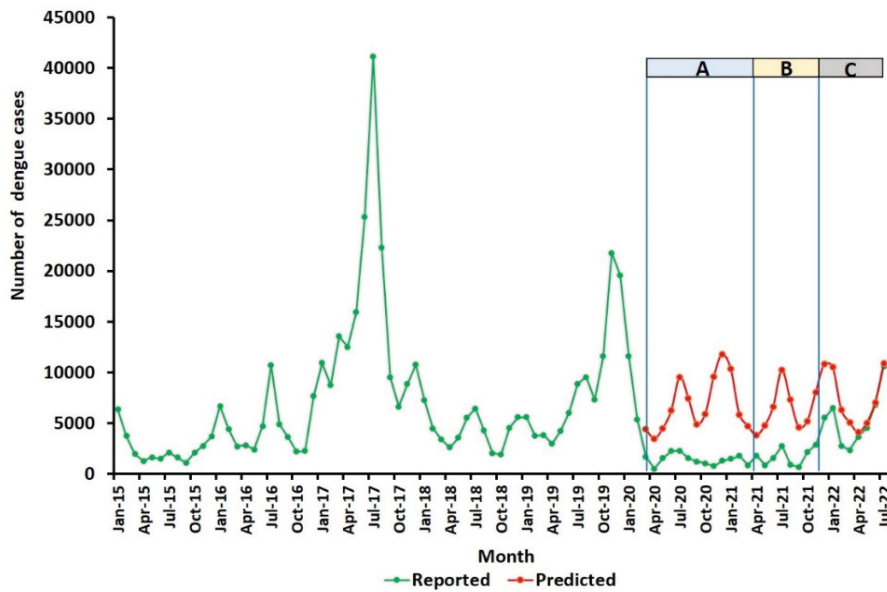


Figure 4: Numbers of actual and predicted dengue cases in the Jaffna district during COVID-19 movement restrictions. Severe restrictions on movement of people were in place from 1 March 2020 to 30 April 2021 (period A) to lower COVID-19 transmission. These were variably eased and reimposed from 1 May 2021 until 22 November 2021 (period B), but removed altogether with the full opening of all schools from 22 November 2021 onward (period C). Reproduced with permission under the creative commons licence from [30].

>100,000 cases annually in Sri Lanka. Despite overwhelming published evidence beginning with the first demonstration of salinity tolerant *Aedes* vectors in Sri Lanka in 2011 [5] and subsequently in other countries [12-17], Sri Lanka's Ministry of Health has been slow to target BW collections in coastal areas in its dengue control program. The WHO and CDC guidelines for controlling dengue however continue to only focus on FW habitats of the *Aedes* vectors [1-4]. Because the WHO guidelines serve as a model for many countries, their modification to additionally target BW habitats of the two vectors can be an important advance globally for the more effective control of dengue and other arboviral diseases. The documented preimaginal development of both *Ae. aegypti* and *Ae. albopictus* in BW habitats in coastal areas of the state of Florida [13], and *Ae. aegypti* in neighbouring Mexico [15], suggests that modifying the existing CDC guidelines [2] to target coastal BW habitats of the two vectors will likewise benefit the control of dengue and other arboviral diseases in the US.

Understanding the implications of the reduced *Aedes* vector densities and dengue incidence observed during the COVID-19 lockdown for dengue control measures

Public health measures that severely curtailed the movement of people to reduce COVID-19 transmission during the period from 2020 to 2022, termed lockdown, were initially predicted to adversely affect mosquito control programs and increase the incidence of diseases like malaria

and dengue in endemic countries [26]. A significant increase in the incidence and mortality from malaria during the COVID-19 lockdown was indeed reported in Zimbabwe [27]. A small increase in dengue incidence was also reported from Singapore [28] which is a country that employs stringent larval source reduction measures in both public places and residences to control dengue transmission. However, dengue incidence markedly decreased in all districts of Sri Lanka during the COVID-19 lockdown [29-32]. An 89% reduction in the number of predicted dengue cases during the most drastic lockdown period from March 2020 to April 2021 in the northern Jaffna district (Figure 4) was accompanied by an 89% drop in *Aedes* larvae collected from ovitraps in Jaffna city [29,30].

Dynamics of disease transmission by vector mosquitoes in a non-immune population is simply described by the Ross-MacDonald equation [33] which can be usefully applied to dengue transmission in the present context. This equation relates the number of secondary infections generated from a single infected person (R_0) to vector parameters as follows:

$$R_0 = ma^2\alpha\beta p^n / r[-\log_e(p)]$$

m= ratio of the number of vector mosquitoes to the number of humans;

a= average number of human blood meals taken by a mosquito in a day;

α =probability of transmission of pathogen from an infected human to a biting mosquito;

β = probability of transmission of a pathogen from an infected mosquito to a non-immune human during feeding;

p =daily probability of survival of the mosquito vector;

n =duration in days from infection of a biting mosquito until the mosquito becomes capable of infecting humans after the pathogen undergoes obligatory development in the mosquito, also termed the extrinsic incubation period;

r = recovery rate in humans (inverse of the average duration of infectiousness in days).

The anthropophilic *Ae. aegypti* and partially anthropophilic *Ae. albopictus* vectors are daytime feeders [1-4,9,34]. The two vectors are highly prevalent in premises of schools, hospitals, government offices, transport hubs, and factories in Sri Lanka [9,35]. The closure of schools and offices, as well other forms of restrictions on the movement of people outside of residences, can therefore be expected to reduce blood feeding by the two vectors, particularly *Ae. aegypti*, leading to a reduction in 'a' in the equation. Any reduction in blood meals will result in reduced oviposition and decreased vector densities, manifesting as reductions in 'm' and 'p'. Lower values for 'a', 'm', and 'p' will diminish R_0 , which will be particularly impacted by its exponential relationship with 'a' and 'p'. R_0 is directly related to the rate of dengue transmission and therefore the number of dengue cases in the population. Reduced oviposition as a result of decreased blood feeding is consistent with diminished larval collections from ovitraps in Jaffna city [29,30], which was independently also observed in the western Colombo district [32], during the lockdown in Sri Lanka.

In particular, diminished access of *Aedes* vectors to blood meals in public places like schools, transport hubs, shops, temples and churches during the COVID-19 lockdown have been postulated to reduce vector densities and vector survival and therefore dengue transmission [29,30]. Both infection of uninfected *Aedes* vectors through feeding on infected persons, and infection of uninfected persons by infected *Aedes* vectors in new locations are promoted by population mobility, and may have additionally contributed to the reduced dengue incidence observed during the COVID-19 lockdown. Dengue and malaria incidences fell by 75% and 46% respectively during the 2020 lockdown in India [36], a country with similar dengue epidemiology and mosquito vector control programmes to Sri Lanka. Corresponding statistics for malaria are not applicable in Sri Lanka because malaria was eliminated from the island in 2013 [37]. The early expectation of epidemiologists, and the WHO, that the incidence of dengue and malaria will increase due to a collapse of vector control programmes during the COVID-19

pandemic [26], was therefore not borne out in India and Sri Lanka. From the perspective of more effective dengue control in Sri Lanka, India and other countries with similar dengue epidemiology, it would appear that this prevalent view [26] detracts from experimental findings [29,30] which strongly suggest that dengue control measures involving *Aedes* vector larval source reduction measures need to be more stringently applied than at present in public places where people congregate.

Conclusions

It is suggested that greater awareness of the relevant scientific findings by pertinent national and international organisations and their adoption of appropriate measures can improve the control of dengue and other arboviral diseases. Beneficial measures can include promoting further epidemiological studies to confirm the importance of the reported findings and modifying influential national and international guidelines for the control of *Aedes* vectors.

Malaria

The WHO in its latest World Malaria Report estimated 249 million cases of malaria occurred worldwide in 2022 (an increase of 5 million over 2021) and 608,000 deaths from malaria worldwide [38]. All known species of *Plasmodium* parasites that cause human malaria are transmitted by several different species of *Anopheles* mosquitoes [39].

Understanding the implications of *Anopheles* vectors adapting to salinity in coastal areas for malaria transmission

Some salinity-tolerant *Anopheles* that transmit malaria parasites in coastal areas have evolved into distinct species as a result of their reproductive isolation. These include *An. farauti* in Australasia, *An. sudaicus* in Asia, *An. melas* and *An. merus* in Africa, as well as *An. aquasalis* and *An. albimanus* in the Americas [23-25]. It was recently observed for the first time that *An. culicifacies*, the principal rural FW vector of malaria in South Asia, can also lay eggs and undergo preimaginal development in BW of up to 4 gL⁻¹ salt in coastal swamps of eastern Sri Lanka [40] and the Jaffna peninsula [7,41]. It remains to be established whether *An. culicifacies* similarly develops in coastal BW habitats in other South and Southeast Asian countries. Larval source reduction was previously an important component of efforts to control or eradicate malaria but this is no longer the case [38]. However, this position needs to be reconsidered, and anopheline vectors in coastal areas monitored more closely, because global warming leading to a rise in sea levels can expand BW habitats for existing salinity-tolerant anopheline malaria vectors in coastal areas and additionally cause FW anopheline vectors to adapt to develop in coastal BW [23-25].

Appreciating the relevance of salinity adaptation and societal conflicts in the recent rapid range expansion of the malaria vector *Anopheles stephensi*

Anopheles stephensi, the principal urban vector of malaria in South Asia, was first detected in Mannar island, Sri Lanka (Figure 1) in 2017 [42,43]. This was postulated to be a consequence of its rapid range expansion from northern India to southern India by a predominantly coastal route [44]. *Anopheles stephensi* has been observed to develop in BW of up to 3.5 gL⁻¹ in cement water storage tanks and domestic wells in different locations within the coastal city of Jaffna as well as Mannar island (Figure 1) [11,42,43,44]. It seems probable that the pre-adaptation of *An. stephensi* to similar BW collections in the neighbouring coast of Tamil Nadu state in South India, and the movement of refugees and combatants in boats across the 64 -137 km-wide Palk Strait separating Tamil Nadu from the Jaffna peninsula contributed to the arrival of *An. stephensi* in northern Sri Lanka [44]. *Anopheles stephensi* has also recently expanded its range westwards to the Arabian Peninsula and after that to Northeast Africa with coastal zones playing a prominent role in this process [38,44]. Further expansion of the range of *An. stephensi* to West and East Africa was confirmed in 2023 [38]. It is reasonable to

postulate that, as in Sri Lanka [44], adaptation to salinity as well as wars in Yemen, Eritrea, Ethiopia, Sudan and Somalia that caused the collapse of societal infrastructure, governments and malaria vector control programs, and resulting in the large-scale movement of refugees, had a major role in the spread of *An. stephensi* and a consequent increase in malaria transmission [38].

Conclusions

Scientific findings that demonstrate adaptation of FW malaria vectors to salinity suggest that the extension of control measures to BW preimaginal habitats is important for controlling malaria in coastal areas [23,40]. This can also increase malaria transmission inland because BW-developing vectors can act as bridging vectors in adjoining inland locations [21]. It is suggested that greater awareness of relevant scientific findings, facilitation of epidemiological studies to further evaluate the findings and promotion of malaria control measures in coastal areas by pertinent national and international malaria institutions are needed. However, reducing the impact of wars and movement of refugees on malaria control is a more difficult-to-address societal problem.

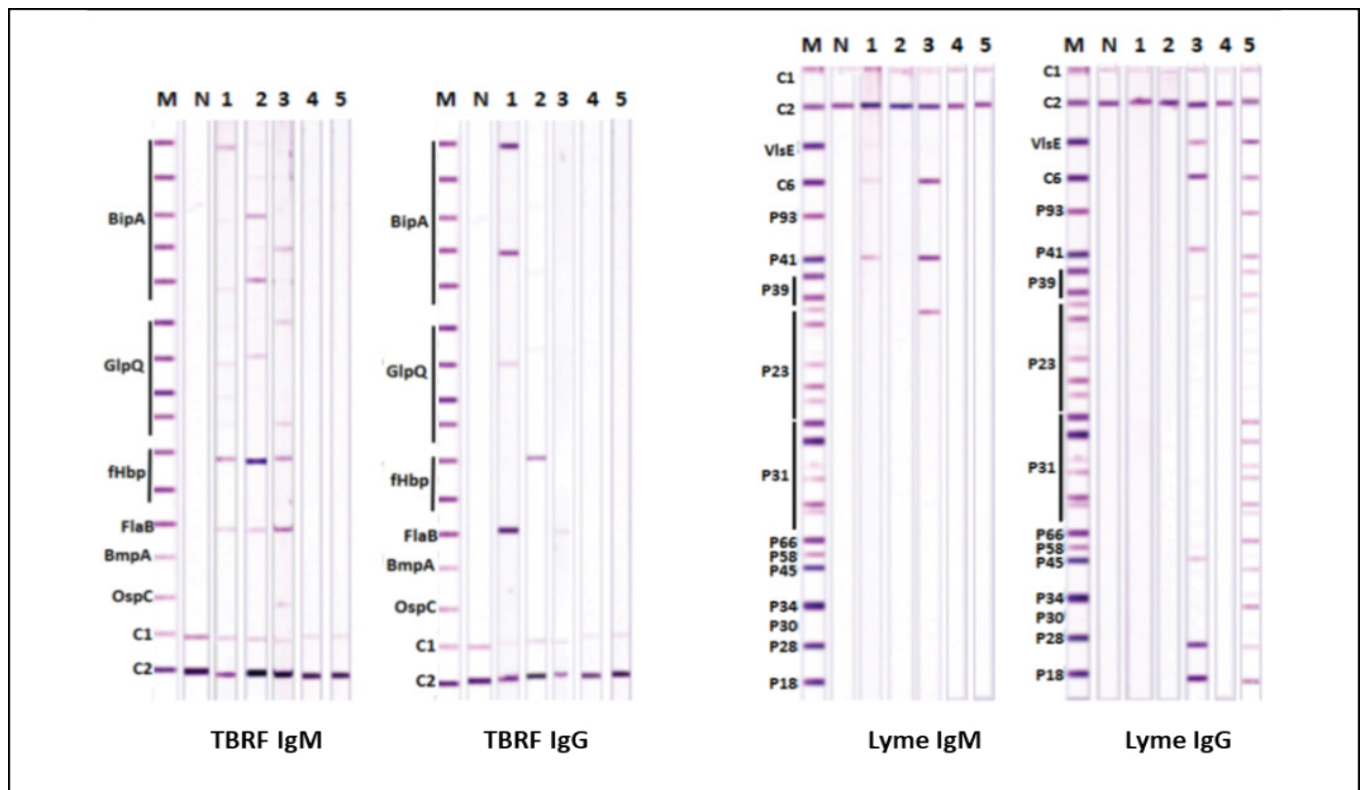


Figure 5: Representative TBRF and LD IgM and IgG IBs with five sera from patients with LD-like symptoms. Sera of both patients in lanes 1 and 2 were only positive in TBRF IBs. Serum in lane 3 was positive in both TBRF and LD IBs. Serum in lane 4 was negative in both IBs. Serum in lane 5 was only positive in LD IBs. The detection of either IgM or IgG antibodies as shown in Figure 5 provided greater sensitivity than detecting either IgM or IgG alone. The different LDB and RFB antigens used in LD and TBRF IBs are described elsewhere [51,52]. N-negative control. Reproduced with permission under the creative commons licence from [52].

Tick-borne Borreliosis

The pathogen causing Lyme disease (LD) was first identified in vector ticks in 1982, and then in US patients in 1983, as a spirochete bacterium later named *Borrelia burgdorferi*. *Borrelia burgdorferi sensu stricto* (*Bbss*) is the principal species responsible for LD in the US [45,46]. Other species of the genus *Borrelia* termed Lyme Disease *Borreliae* (LDB), or alternatively *Borrelia burgdorferi sensu lato*, are now known to cause LD in many temperate zone countries [45,46]. Some clinical manifestations of LD are shared with tick-borne relapsing fever (TBRF) caused by a different group of *Borrelia* species termed relapsing fever *Borreliae* (RFB) [45,47], and indeed with non-borrelial tick-borne diseases [48]. TBRF is prevalent in both tropical and temperate climates in many parts of the world [45,47].

Importance of serological tests in the diagnosis of LD and TBRF and the implications of recent findings with the tests

In the absence of distinct pathognomonic features, other than erythema migrans at the site of a tick bite which is frequently not noticed, a diagnosis of LD relies heavily on laboratory confirmation of infection. Because LDB are often present at low concentrations in blood, the detection of antibodies in patient sera became the preferred laboratory diagnostic method for LD [45,49]. The recommendation from the US National Conference on Serologic Diagnosis of Lyme Disease meeting in 1994 of a standard two-tier test (STTT) for the serological diagnosis of LD was an important diagnostic advance [49]. The first tier of the STTT is an enzyme immunoassay (EIA) or immunofluorescence assay (IFA) on whole *Bbss* cell antigens, followed by a second-tier confirmatory western blot (WB) on whole *Bbss* cell lysates for sera that give positive or equivocal results in the first-tier test [49]. The rationale for the STTT was that the first tier EIA or IFA was highly sensitive but inadequately specific, while the second tier WB was highly specific for detecting serum antibodies to LDB [49]. Drawbacks to STTTs include the need for the cumbersome WB procedure and variable sensitivity for detecting infections with LDB species other than *Bbss*, both of which can be overcome by using relevant pure proteins as target antigens [45]. As a result, the CDC has been approving modified two-tier tests (MTTTs) amenable to machine reading of results in the US since 2019 [50].

Line immunoblots (IBs), based on pure proteins produced by recombinant DNA technology and applied as lines on blotting media strips, have supported the diagnosis of LD in European laboratories from the beginning of this century [45]. LD IB tests used as potential single tier tests had comparable sensitivity and specificity to STTTs and were also able to detect antibodies against common European LDB species [45,51]. LD IB tests have led to the development of analogous TBRF IB tests that detect RFB-specific antigens

[45,52]. The use of TBRF IBs to test patients identified with LD-like symptoms in Ukraine, Australia and the US strongly suggested the many of them had TBRF and not LD [45,52]. Testing of patient sera in parallel in both LD and TBRF IBs, as illustrated in Figure 5, may therefore provide a more definitive diagnosis of tick-borne borreliosis worldwide [45,52].

The CDC estimated that approximately 476,000 persons were treated every year for LD in the US during the period 2010-2018 [53]. The number LD cases in western Europe was estimated to be >200,000 per year and increasing every year [54]. The CDC reported 483 cases of TBRF for the entire period of 1990 to 2011 in the US that were confined mainly to the western US states [47], contrasting with other findings that suggest a much greater incidence and broader distribution within the US [52].

Conclusions

Many myths about LD propagated by the print, broadcast and internet media have long compromised its diagnosis and treatment [55]. LD and TBRF in their early stages are readily amenable to antibiotic treatment. However, symptoms and pathology in chronic LD are complex and some cases of chronic LD are difficult to treat [45,46]. Recent findings discussed here suggest a need to re-evaluate the incidence of LD and TBRF in the US and other countries. This would involve promoting further research to verify recent findings and greater coordination between scientific communities working on the diagnosis of LD and TBRF, by relevant national institutions like the CDC in the US.

COVID-19

The WHO estimated 774 million cases of COVID-19 due to infection with the SARS-CoV-2 virus and 7 million deaths worldwide up to the end of 2023 [56]. Vaccines against COVID-19 were rapidly developed after COVID-19 was first identified in 2019. COVID-19 vaccines provided the urgently needed initial immunity in the global population to withstand the severe consequences of the disease. One of the first to complete clinical trials and receive regulatory approval was the University of Oxford-Astra Zeneca ChAdOx1 nCoV-19 vaccine, which utilized a recombinant chimpanzee adenovirus vector expressing the spike protein of SARS-CoV-2 as an immunogen [57]. This vaccine was offered for use on a not-for-profit basis for the duration of the pandemic, and also licensed to be manufactured inexpensively for resource-constrained countries at the Serum Institute of India.

Understanding the impact of vaccination during the COVID-19 pandemic

During the first year of COVID-19 vaccination from December 2020 to December 2021, 55.9% of the global population was estimated to have received one dose of

a vaccine, 45.5% two doses, and 4.3% a third booster immunisation [58]. Based on officially reported COVID-19 deaths, 14.4 million (95% confidence interval 13.7–15.9), and alternatively the excess mortality data, 19.8 million (95% interval 19.1–20.4) deaths, were estimated to have been averted by vaccination in 185 countries over this one-year period [58]. Similar findings were reported at the country level from the US [59] and Israel [60]. Vaccination ameliorated the serious effects of SARS-CoV2 infections in persons who had not previously had COVID-19, and served to enhance population immunity that minimized severe disease and mortality. Thus, COVID vaccines had a major beneficial impact on the early course of the pandemic and they continue to be used to boost immunity in elderly and immunocompromised persons at the present time. More lives would have been saved if resource-constrained countries had better early access to vaccines [58], some governments had not delayed beginning vaccinations or been more transparent about the local COVID-19 situation, and more people had not resisted receiving the vaccine due to cultural perceptions and misconceptions spread through the print, broadcast and internet media [61,62].

Understanding the consequences of differential susceptibility of population groups to SARS-CoV-2 infection

Increased susceptibility to SARS-CoV-2 infections and consequent higher mortality during the temperate zone winter in persons with a genetic ancestry in warm tropical countries, was widely attributed to socio-economic factors but not a likely weaker early immune response in the upper respiratory tract for which there is now increasing evidence [63-67]. Timely recognition of this could have led to the implementation of appropriate public health and clinical measures that might have reduced infections, morbidity and mortality during the COVID-19 pandemic among vulnerable immigrant communities living in temperate zone countries.

Conclusions

Media-propagated misinformation on COVID-19 vaccines and delays in administering vaccines in some countries increased morbidity and mortality worldwide. Further investigations into varying SARS-CoV-2 infectivity among different population groups may be useful for minimising morbidity and mortality. It is suggested that these issues need to be addressed at the appropriate national and international levels.

General Conclusions

Some of the societal shortcomings affecting the control of COVID-19, dengue, malaria, and tick-borne borreliosis, highlighted in this article, will have resulted in avoidable morbidity and mortality. Two of the identified societal drawbacks appear to be shared between

diseases: (i) the need for greater cognizance of scientific advances and then timely initiation of appropriate responses on the part of pertinent national and international institutions. More extensive investigations and scientific discussion may be needed to fully evaluate the relevant scientific findings cited here but this also need to be facilitated by national and international institutions with the relevant responsibilities; (ii) misleading information in the print, broadcast and internet media, and the potential dangers of advanced computer technology in facilitating such misinformation. The general issue of misinformation in science, its consequences and the steps needed to address it, were recently highlighted in the journal Nature [62]. Misinformation also negatively impacts the control of other infectious diseases. For example, misperceptions and misinformation spread through social internet media have led to reduced vaccine uptake not only in COVID-19 as discussed here [61] but also measles [68]. This has caused widespread resurgence of measles [69].

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Abbreviations

AFM- atomic force microscopy; CDC – US Centres for Disease Control and Prevention; COVID-19 - coronavirus infectious disease 2019; EIA- enzyme immunoassay; IFA- immunofluorescence assay; L1-L4 - first to fourth instar larval stages; LC₅₀- concentration producing 50% lethality; LD - Lyme disease; LDB - Lyme disease *Borreliae*; MTTT- modified two-tier test; RFB - relapsing fever *Borreliae*; TBRF - tick-borne relapsing fever; SARS-CoV-2 - severe acute respiratory syndrome coronavirus 2; SEM - scanning electron microscopy; STTT - standard two-tier test; TEM - transmission electron microscopy; WB - western blot; WHO - World Health Organization.

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