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Article

Societal Factors Constraining the Control of COVID-19 and Mosquito and Tick-Borne Diseases

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Abstract: Advances in biological sciences have been applied in medicine, agriculture and industry with great benefit. Some recent trends in society, governance structures and communications, however, appear to be hampering the use of new scientific findings for controlling infectious diseases. These limitations are illustrated with examples related to (i) the adaptation of fresh water mosquito vectors of major arboviral diseases to salinity in coastal areas with consequences for disease transmission, (ii) understanding the implications of reduced dengue transmission during the COVID-19 lockdown for dengue control, (iii) causes underlying the rapid spread of the malaria vector *Anopheles stephensi* in South Asia and Africa, (iv) the application of serodiagnostic techniques for Lyme disease and tick-borne relapsing fever caused by tick-borne bacteria of the genus *Borrelia*, and (v) COVID-19 prevention.

Keywords: *Aedes aegypti; Aedes albopictus; Anopheles culicifacies; Anopheles stephensi;* borreliosis; dengue; climate change; COVID-19; lyme disease; malaria; salinity adaptation in mosquito vectors; serodiagnosis; tick-borne relapsing fever; vaccines

1. Introduction

The use of other living organisms and their products for human benefit has a very ancient origin. Identification of herbal medicines, selection of wild cereal crops to form cultivated varieties, domestication of goats, sheep and cattle, cultivation of cotton, and fermentation of plant products to form alcoholic beverages are some examples [1]. However, elucidation of the structure of DNA and proteins in the middle of the 20th century spawned the science of molecular biology which has been applied in innovative ways in medicine, agriculture, and industrial production for human benefit. For example, biotechnology, defined by the European Federation of Biotechnology in 1981 as 'the integrated use of biochemistry, microbiology and chemical engineering in order to achieve the technological application of the capacities of microbes and cultured cells' [1], has created useful products such as monoclonal antibodies for clinical therapy of COVID-19, reagents for the laboratory diagnosis of infectious diseases [2-4], and the CRISPR-Cas9 gene editing technology for advancing human medicine, agriculture and animal husbandry [5].

Some societal limitations that presently have an impact on human well-being are well known. Two prominent examples are the (i) rapid expansion of human populations and improvements in their quality of life, largely attributable to science-based improvements in healthcare and food production, but leading also to the unsustainable use of the planet's biotic and abiotic resources, and (ii) continuing high levels of greenhouse gas emissions and environmental pollution, causing many undesirable effects, including global warming. While the two factors also influence the prevalence of infectious diseases, less-well understood societal factors that limit application of recent advances in biological sciences for controlling infectious diseases have emerged. These constraints are discussed with specific examples from (i) the transmission of dengue by *Aedes* mosquitoes, (ii) the transmission of malaria by the urban malaria vector *Anopheles stephensi*, (iii) the application of serological techniques for the laboratory diagnosis of Lyme disease and tick-borne relapsing fever borreliosis, (iv) understanding immunity to SARS-CoV-2 and the delivery of COVID-19 vaccines.

2. Development of *Aedes* mosquito vectors in coastal brackish water and its impact on the control of dengue and other arboviral diseases

Aedes aegypti mosquitoes are the principal vectors of human arboviral diseases, including dengue, chikungunya, yellow fever and Zika, in tropical and sub-tropical countries [6-8]. 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 [6-8]. Both Aedes species are widely regarded to lay eggs and undergo preimaginal development only in fresh water (FW) habitats containing <0.5 gL⁻¹ salt, so that the present World Health Organization (WHO) [6,7] and US Centres for Disease Control and Prevention (CDC) [8] guidelines for larval source reduction through applying larvicides and elimination of preimaginal habitats are only directed towards fresh water habitats. Larval source reduction measures are important worldwide for controlling Aedes vectors, compared to the spraying of adulticides indoors and the use of insecticide impregnated bed nets which are effective against Anopheles mosquito vectors of malaria. This is because the two Aedes species, in contrast to the *Anopheles* vectors, tend to blood feed on humans outdoors during the day. Most countries follow WHO recommendations for controlling arboviral diseases, including dengue which is the most prevalent arboviral disease worldwide with 5.2 million annual cases reported to the WHO in 2019 but with a higher estimated incidence of 100 – 400 million cases worldwide [6-8]. The WHO recommends measures to minimize or eliminate fresh water 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 fresh water storage containers which constitute important Aedes larval habitats in the tropics, and space spraying with adulticides to control dengue epidemics [7,9].

Aedes aegypti and Ae. albopictus were first reported 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 defined as containing < 0.5, 0.5–30 and > 30 gL⁻¹ salt, respectively [10-15].

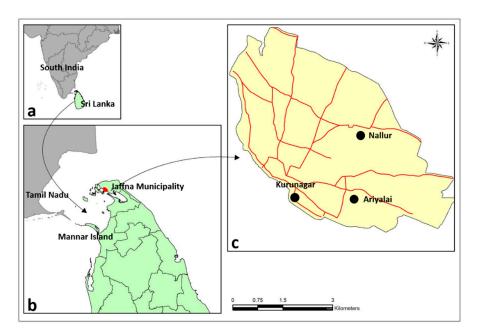


Figure 1. (a) Map showing the location of Sri Lanka in relation to South India; (b) the relative locations of the Jaffna peninsula, Mannar island and Jaffna city within Sri Lanka; (c) sites within Jaffna city where *Anopheles stephensi* (discussed in section 4) larvae are found. Reproduced with permission under the creative commons licence from [16].

The preimaginal development of *Ae. aegypti* and *Ae. albopictus* in BW has since been reported from the coastal areas of other countries including Brunei Darussalam [17], the US [18], Brazil [19],

Mexico [20], Indonesia [21], and India [22]. Typical BW habitats of *Ae. aegypti* are BW accumulations in beach debris, fishing boats, and coastal wells, as well as discarded containers in swamps, stagnant surface drains, surface ground water and household containers in coastal areas [10-15,17-22]. Some BW collections where *Ae. aegypti* larvae were found in Jaffna city and the Jaffna peninsula are illustrated in Figure 2.



Figure 2. BW habitats of *Ae. aegypti* in the Jaffna peninsula. 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 [10].

BW-derived *Ae. aegypti* and *Ae. albopictus* larvae in the Jaffna peninsula were more salinity-tolerant, possessing higher LC₅₀ for salt than the corresponding FW-derived larvae from the Sri Lankan mainland as shown in Figure 3 [10,15,23]. *Aedes albopictus* was observed to be more salinity tolerant than *Ae. aegypti* at both locations (Figure 3).

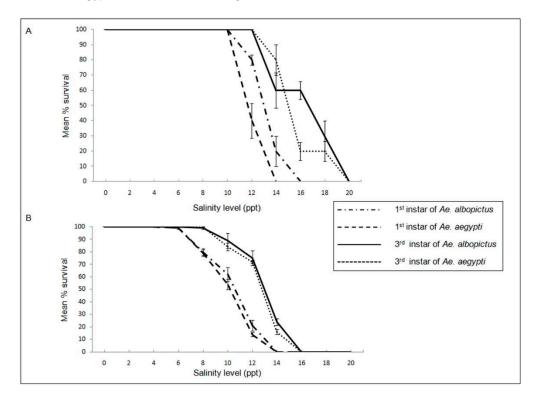


Figure 3. Effect salinity on *Ae. aegypti* and *Ae. albopictus* from (A) coastal Jaffna peninsula and (B) mainland Sri Lanka on the L1and L3 larvae to adult transformation. L1 and L3 refer to first and third

instar larvae respectively. Ppt – parts per thousand or gL⁻¹. Reproduced with permission under the creative commons licence from [10].

Further investigations on laboratory-maintained colonies demonstrated that, although they remained reproductively compatible, BW-adapted or salinity-tolerant *Ae. aegypti* differed from FW *Ae. aegypti* significantly in several important features that are summarized in Table 1. These structural and physiological differences have been suggested to be related to the development of salinity tolerance in BW *Ae. aegypti*.

Table 1. Differences between salinity-tolerant (BW) Ae. aegypti and FW Ae. aegypti.

Characteristic	Differences	Cited References
LC50 for salt	Significantly higher LC50 in BW Ae.	
	aegypti for the L1 and L3 to adult transition. An inheritable	[10, 15, 23]
	characteristic	
Osmoregulatory anal papillae in L3 larvae	Significantly larger anal papillae in BW <i>Ae. aegypti</i> . An inheritable characteristic	[24]
Gene expression in mid-L4 larvae	Marked differences, particularly in	[25]
	genes for cuticle proteins, and others associated with cuticle synthesis	
Protein composition of L4 cuticles	Marked differences compatible with the gene expression data	[25]
Cuticle structure by TEM	Thicker cuticles in L4 larvae and adult abdomen with more prominent endocuticles and exocuticles in BW Ae. aegypti	[25]
Surfaces of shed L3 and L4 cuticles	More pronounced surface undulations in BW <i>Ae. aegypti</i> cuticles by AFM and SEM	[15]
Egg sizes	Significantly smaller eggs in BW Ae. aegypti	[15]
Surfaces of eggs by AFM and SEM	BW Ae. aegypti egg surfaces were significantly less elastic by AFM, with more undulating surfaces seen by AFM and SEM	[15]
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	[15]
Susceptibility of L3 and L4 to the common larvicide	BW Ae. aegypti were significantly more resistant than FW Ae. aegypti in a 24h assay	[15]

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

All the salinity-adaptive structural and molecular changes seen in *Ae. aegypti* are expected to be paralleled in the secondary arboviral vector *Ae. albopictus*, as well as other FW mosquito vectors that have adapted to salinity, *e.g.*, the malaria vector *Anopheles culicifacies* discussed in section 4.

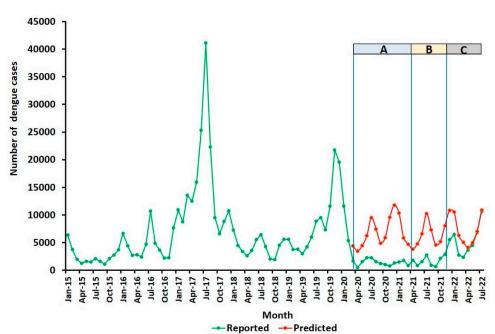
The euryhaline nature of salinity-tolerant *Aedes* vectors in coastal areas and their neglect in vector control programs, allows them to serve as arboviral reservoirs in coastal areas and function as bridging vectors for adjoining inland areas, thereby enhancing arboviral disease transmission and facilitating epidemics [26]. As a consequence, it is 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 [27, 28]. 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 [29, 30]. It is therefore important that in coastal zones throughout the world there is a need to (i) extend larval source reduction efforts also to the BW habitats of *Aedes* vectors, and (ii) monitor the efficacy of widely-used larvicides in coastal areas [15].

Dengue is the most prevalent arboviral disease worldwide and causes >100,000 cases annually in Sri Lanka. Despite overwhelming published evidence for more than a decade following the first demonstration of salinity tolerant *Aedes* vectors in Sri Lanka in 2011 [10], the country's Ministry of Health has only recently begun to target BW collections in coastal areas in its dengue control program. However, the WHO and CDC have yet to modify their guidelines for controlling dengue and other arboviral diseases, which continue to focus solely on FW habitats of the *Aedes* vectors [6-9].

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

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 widely expected to adversely affect mosquito control programs and increase the incidence of diseases like malaria and dengue in endemic countries [31]. A significant increase in the incidence and mortality from malaria during the COVID-19 lockdown was indeed reported in Zimbabwe [32]. A small increase in dengue incidence was also reported from Singapore [33] which is a country that employs stringent larval source reduction measures in both public places and residences to control dengue transmission.

However, the incidence of dengue incidence markedly decreased in all districts of Sri Lanka during the COVID-19 lockdown [34-37]. 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 also accompanied by an 89% drop in *Aedes* larvae collected from ovitraps in Jaffna city [34,35].



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Dynamics of disease transmission by vector mosquitoes for a non-immune population is described by the Ross–MacDonald equation [30,38] 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 (R₀) 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 anthropophagic *Ae. aegypti* and partly anthropophagic *Ae. albopictus* vectors are daytime feeders [6-10,39] that are highly prevalent in premises of schools, hospitals, government offices, transport hubs, and factories in Sri Lanka [14,40]. 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 reduced values of 'm' and 'p'. Lower values for 'a', 'm', and 'p' will diminish R₀, which will be particularly impacted by its exponential relationship with 'a' and 'p'. R₀ 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 [34,35], which was also independently observed in the western Colombo district [36], during the lockdown in Sri Lanka.

In particular, diminished access of Aedes vectors to blood meals in public places like schools, transport hubs, shops, and temples during the COVID-19 lockdown were postulated to reduce vector densities and vector survival and therefore dengue transmission [34,35]. Additionally, infection of uninfected Aedes vectors through feeding on infected persons, and infection of uninfected persons by infected Aedes vectors in new locations are both promoted by population mobility, and could have contributed to reduced dengue incidence during the COVID-19 lockdown. Dengue and malaria incidences fell by 75% and 46% respectively during the 2020 lockdown in India [41], a country with similar dengue epidemiology and mosquito vector control programmes to Sri Lanka. Statistics for malaria were not available for Sri Lanka because malaria had been eliminated from the island in 2013 [42]. The early expectation of epidemiologists, held also by the WHO, that the incidence of dengue and malaria will increase due to a collapse of vector control programmes during the COVID-19 pandemic [31], 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 early prevalent view [31] detracts from experimental findings [34,35] which strongly suggest that dengue control measures involving Aedes vector larval source reduction need to be more stringently applied in public places where people congregate.

4. Adaptation of fresh water *Anopheles* malaria vectors to salinity and its consequences for malaria control

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 Australia and neighbouring countries, *An. sundaicus* in Asia, *An. melas* and *An. merus* in Africa, as well as *An. aquasalis* and *An. albimanus* in the Americas [28-30]. 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 [43] and the Jaffna peninsula [44,45]. It is possible that *An. culicifacies* may similarly develop in coastal BW habitats of other South and Southeast Asian countries. Larval source reduction was an important component of efforts to control or eradicate malaria in the past no longer considered to be the case by the WHO [46]. However, this position needs to be reconsidered, and the performance of further vector surveys supported, because global warming leading to a rise in sea levels can increase brackish water habitats for anopheline malaria vectors in coastal areas [28-30].

Anopheles stephensi, the principal urban vector of malaria in South Asia, was first detected in Sri Lanka as having arrived from India to Mannar island (Figure 1) in 2017 [47]. Anopheles stephensi was later observed to develop in BW of up to 3.5 gL-1 in cement water storage tanks and domestic wells in different locations within Jaffna city (Figure 1) as well as Mannar island [16,47,48]. It postulated that its adaptation to similar BW habitats in in neighbouring coast of Tamil Nadu state in South India, and the movement of refugees and combatants in boats during the 1983-2009 civil war in Sri Lanka, as well as monsoonal winds across the 64-137 km-wide separating Palk strait (Figure 1) may have facilitated this expansion in the range of An. stephensi [45,48]. Anopheles stephensi 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 [46,48]. Further expansion of the range of An. stephensi to West and East Africa was confirmed in 2023 [46]. It seems reasonable to postulate that, as in Sri Lanka [48], civil wars in Yemen, Eritrea, Ethiopia, Sudan and Somalia that were accompanied by the collapse of societal infrastructure, governments and vector control programs, as well as the movement of refugees, had a major role in the spread of An. stephensi and the consequent increased malaria transmission in the Arabian Peninsula and Africa [46].

5. Laboratory tests supporting clinical diagnosis of Lyme disease and tick-borne relapsing fever

The pathogen causing Lyme disease (LD) was first identified in ticks in 1982, and then in human patients in the US in 1983, to be a spirochete bacterium later named *Borrelia burgdorferi*. *Borrelia burgdorferi* sensu stricto (Bbss) is the principal species responsible for LD in the US [4,49]. 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 [4,49]. 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) [4,50], and indeed non-borrelial tick-borne diseases [51]. TBRF is prevalent in both tropical and temperate climates in many parts of the world [4,50].

In the absence of distinct pathognomonic features, other than erythema migrans at the site of a tick bite which often goes unnoticed, 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 has become the preferred laboratory diagnostic method [4,52]. 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 [52]. 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 [52]. 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 [52]. Drawbacks to STTTs include the need for a cumbersome WB procedure and variable sensitivity for detecting infections

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with LDB species other than *Bbss*, both of which can be overcome by using relevant recombinant proteins as target antigens [4]. As a result, the CDC has been approving modified two-tier tests (MTTTs) amenable to machine reading of results in the US since 2019 [53].

Line immunoblot tests (IBs) based on purified recombinant proteins applied as lines on blotting media strips have been used to support the diagnosis of LD in European laboratories from the beginning of the 21st century [4,54]. LD IB tests used potential single tier tests had comparable sensitivity and specificity to STTTs and were also able to detect antibodies against common European LDB species [54]. LD IBs tests have recently been developed together with analogous TBRF IB tests that detect RFB [4,55]. 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 [4,55]. The parallel use of LD and TBRF IBs, as illustrated in Figure 5, can therefore be expected to be more reliable for diagnosing tick-borne borreliosis worldwide [4,55].

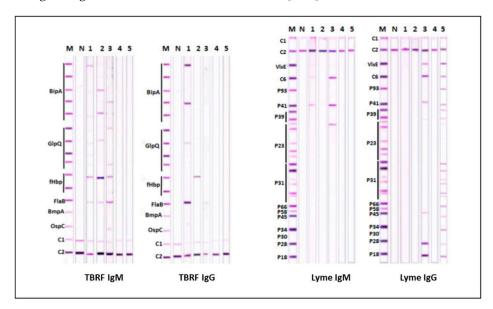


Figure 5. Representative TBRF and LD IgM and IgG IBs with five sera from patients with LD-like symptoms. Sera of both patients in lanes 1 and 2 were only positive in TBRF IBs. Serum in lane 3 was positive in both TBRF and LD IBs. Serum in lane 4 was negative in both IBs. Serum in lane 5 was only positive in LD IBs. The detection of either IgM or IgG antibodies as shown in Figure 5 provides greater sensitivity than detecting either IgM or IgG alone. The different LDB and RFB antigens used in the LD and TBRF IBs are explained elsewhere [54,55]. Reproduced with permission under the creative commons licence from [55].

The CDC estimated, based on commercial insurance claims data, that approximately 476,000 persons were treated every year for LD in the US during the period 2010-2018 [56]. The number LD cases in western Europe was estimated to be >200,000 per year and increasing every year [57]. The CDC reported 483 cases of TBRF during the period 1990-2011 in the US mainly confined to the western states [50], contrasting with other findings that suggest a greater incidence and wider distribution within the US [55]. Limited discourse within the relevant scientific communities and many myths about LD propagated by the print, broadcast and internet media [58], appear to be shortcomings that need to be overcome in the field of human borreliosis.

6. SARS-CoV-2 infectivity and COVID-19 vaccines

The WHO estimated that 774 million cases of COVID-19 had caused 7 million deaths worldwide up to the end of 2023 [59]. Vaccines against COVID-19 were rapidly developed after COVID-19 was first identified to provide the urgently needed initial immunity in the global population to combat the pandemic. One of the first to complete clinical trials was the University of Oxford-Astra Zeneca ChAdOx1 nCoV-19 vaccine utilising a recombinant chimpanzee adenovirus vector expressing the spike protein of SARS-CoV-2 as an immunogen [60]. 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 by the Serum Institute of India as a product named Covishield.

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 [61]. Based on officially reported COVID-19 deaths, 14·4 million (95% confidence interval 13·7–15·9), and alternatively the more reliable excess mortality data, 19·8 million (95% interval 19·1–20·4) deaths are estimated to have been averted by vaccination in 185 countries over this one-year period [61]. Similar findings were reported at the country level from the US and Israel [62,63]. Vaccination ameliorated the serious effects of the spread SARS-CoV2 infections among persons who had not previously had COVID-19, serving 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 [61], 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 [64,65].

Increased susceptibility to infection by SARS-CoV-2 and consequent higher mortality during the temperate zone winter in persons with an 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 [66-70]. 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.

7. Conclusions

Some of the shortcomings in society that appear to negatively impact the control of COVID-19 and the vector-borne infectious diseases Lyme disease, tick-borne relapsing fever, malaria and dengue have been highlighted in this article. The identified drawbacks affect morbidity and mortality due to these diseases. Societal factors may similarly impact other infectious diseases as well. It is possible that more extensive investigations are needed to fully evaluate the relevant scientific findings cited here, but there appears to be little support for this. Governments as well as national and international organizations with relevant responsibilities need to recognize the likely limitations identified here and then address them. It is encouraging in this context that the issue of misleading information in the print, broadcast and internet media, the potential dangers of advanced computer technology in facilitating such misinformation, and assigning liability to the source of misinformation, have recently achieved prominence [65].

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Conflicts of Interest: The author is affiliated to IDFISH and IGeneX which develop and apply diagnostic techniques for tick-borne and other infectious diseases.

Abbreviations

CDC – US Centres for Disease Control and Prevention; COVID-19 – coronavirus disease 2019; EIA- enzyme immunoassay; IFA- immunofluorescence assay; 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

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acute respiratory syndrome coronavirus 2; STTT- standard two-tier test; WB - western blot; WHO-World Health Organization.

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