

Co-feeding in ticks helps transmit tick-borne diseases

Tick-borne diseases such as Lyme disease and tick-borne encephalitis occur when infected ticks feed on humans and livestock. Mathematical modelling to highlight areas and times at high risk of an outbreak has tended to focus on the relationship between the host animals and infected ticks. However, the interactions between ticks of different life stages and hosts of different epidemiological status are also important contributors to overall infestation and infection dynamics. Researchers from the LIAM TBD working group have expanded models to include co-feeding transmission and diapause – a period of suspended development – to provide a wider framework of tick-borne disease modelling.

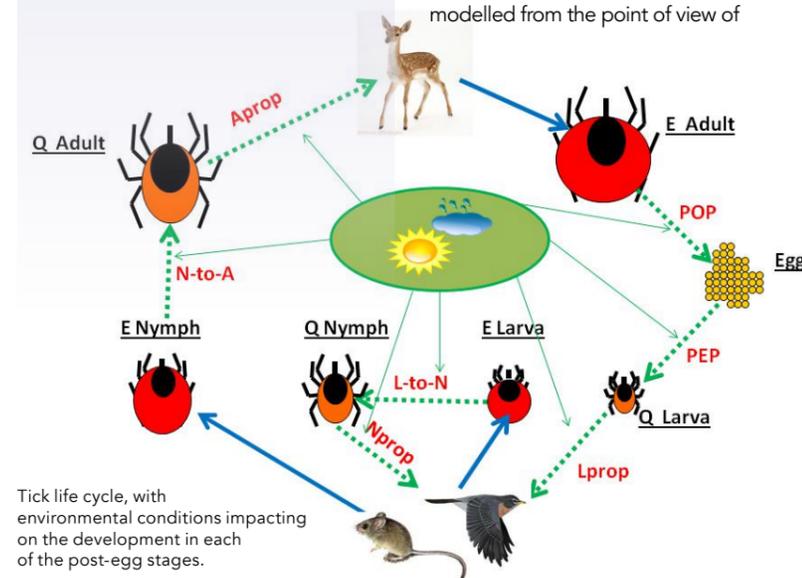
Ticks are arthropods that inhabit woodlands, fields, and shrubs and are well known vectors of diseases such as Lyme disease and tick-borne encephalitis. In Europe and North America, Lyme disease is transmitted to people or livestock bitten by ticks carrying the bacteria *Borrelia burgdorferi* and can be detected by a characteristic ‘bullseye’ rash on the skin, accompanied by a ‘flu-like’ illness. In some cases, Lyme disease causes long-term chronic fatigue, making it of particular concern to people in frequent contact with livestock or habitats of the tick vectors. Public health researchers model the population dynamics of tick populations and disease transmission dynamics in specific areas to try to predict outbreaks of disease and forewarn people of the risks of contact with ticks in these areas.

FROM TICK-HOST TO TICK-TICK-HOST
Historically, tick-borne diseases were modelled from the point of view of

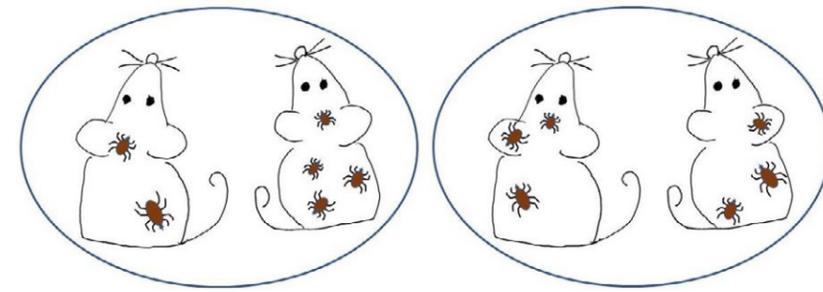
host-pathogen systemic transmission dynamics; that is, how the pathogen becomes widespread in the host which then acts as a reservoir for the vector to become infected. For example, previous models have examined how host density affects transmission, and how different life stages affect the basic reproduction number R_0 (the metric that represents whether a pathogen can persist in a population). However, this does not take account of how individual vectors, such as ticks feeding together, might facilitate pathogen transmission, or how time lags between different vector life stages affects transmission.

Generally, tick populations in nature are known to display annual periodic cycles, and mathematical models have been used to capture the seasonal variation using periodic coefficients to represent the impact of seasonal variations on the non-linear tick-host interaction cycle. Researchers from the LIAM TBD working group have expanded classical host-tick interaction models to include the effect of diapause (the period during which ticks go into a form of hibernation to avoid adverse environmental conditions); but a model that incorporates the transmission through co-feeding of ticks at different life stages was still lacking. Now, these researchers have expanded their models to include the non-systemic transmission route, which brings a paradigm shift from host-tick interactions to tick-tick-host interactions.

Their early version of the co-feeding model showed periodic oscillations that were not always in synchrony with seasonality, demonstrating a separate, additional effect of co-feeding on



Tick life cycle, with environmental conditions impacting on the development in each of the post-egg stages.



Co-feeding transmission efficacy impacted by infestation spatial clustering patterns.

transmission. In more recent work, the group modelled co-feeding in *Ixodes ricinus*, where a susceptible tick acquires the pathogen by feeding concurrently within the same area of skin as infected ticks. By explicitly counting the numbers of susceptible ticks and infected ticks co-feeding on the hosts and examining how it depends on the climate condition, the group was able to identify seasons with high risk of co-feeding transmission.



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in this case one caveat is the hypothesis whether ticks attach to hosts in a random way or whether they occur in clusters. Nevertheless, when integrated into the direct host-vector transmission models, co-feeding and diapause combined add important elements towards a complete framework of tick-borne disease transmission dynamics.

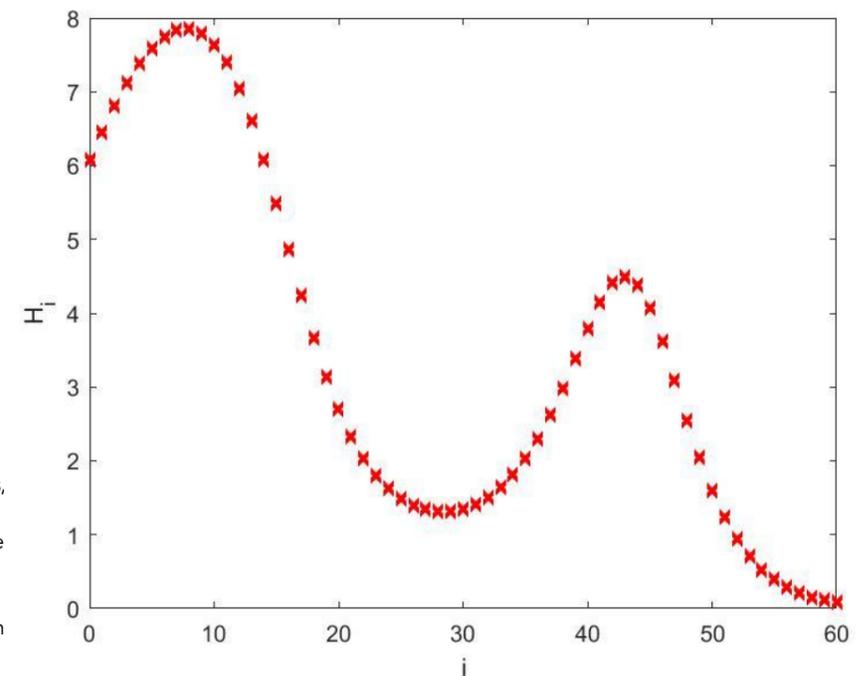
PUBLIC HEALTH INSIGHTS
The LIAM TBD group has brought insights from their co-feeding transmission models

to update the ecological disease models for the transmission in Europe of tick-borne encephalitis (TBE), which affects the central nervous system. In host-vector only models, the estimated R_0 of the tick-borne encephalitis virus (TBEV) was estimated to be <1 in the study area; in other words, in this model the disease should become eradicated from the area. Including co-feeding transmission in the models changed this outcome, possibly explaining why TBE persists in the region.

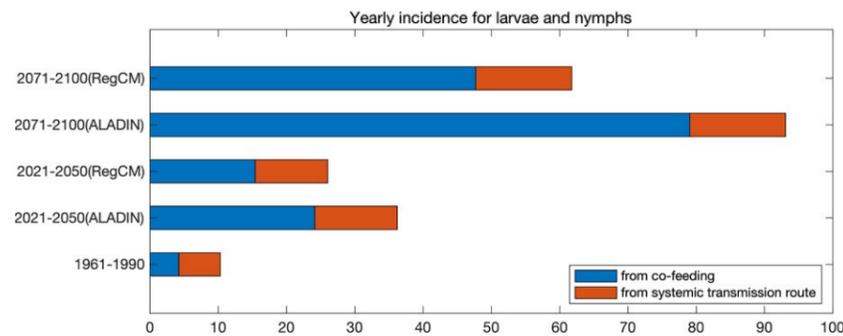
The team also included stochastic (apparently random) reporting of TBE in human populations along with climate data to estimate key parameters such as seasonal encounter rates of humans with ticks, probability of cases being reported, and disease transmission. Surprisingly, despite the R_0 of TBEV increasing over the past few decades, the reported incidences of people falling ill with TBE over the same time-period decreased, suggesting perhaps other public health interventions, such as vaccination programs, had

Researchers model the tick-tick-host interaction and its impact on pathogen transmission in specific areas to try to predict outbreaks of disease and forewarn people.

In their models, the group assumed that the more infected nymphal ticks on the host, the greater the likelihood of a susceptible larval tick becoming infected while co-feeding, providing a vector-to-vector route of transmission independent of the infection status of the host animal. This in turn was strongly affected by individual tick and host behaviours, in this case grooming by the rodent host *Clethrionomys glareolus*, the delays of ticks questing, and the rate at which ticks attached to hosts. By varying specific characteristics of tick and host behaviour, the group observed multiple long-term infection risk scenarios, including extinction of tick population and/or disease transmission, convergence to a single stable equilibrium and, more profoundly, bistability – where the long-term outcome of tick-tick-host interaction depends on the initial infection level. All models necessarily involve some simplification of real natural systems, and



Bistability of infestation dynamics model may explain how tick-host interaction leads to tick-load distribution on hosts.



Projected contributions of co-feeding transmission to the overall incidence can be significant due to climate change.

prevented people becoming infected despite an increasing reservoir of infected ticks in the environment. The expanded models also indicated an influential, albeit relatively smaller, role of co-feeding alongside the more traditional host-vector and seasonal dynamics. This influence was thought primarily to be the 'questing' activity of larval ticks, which itself is strongly seasonally dependent behaviour, again confirming the need for greater complexity in modelling important disease vectors.

TICK-BORNE DISEASE MODELLING AND CHANGING CLIMATE

Modelling vector-borne diseases in general and tick-borne diseases in particular is becoming more pressing and complex with accelerating climate change, which is known to affect many natural biological processes, from flowering and pollination dates to seasonal migrations as well as disease dynamics. For example, in the Czech Republic, ticks are inhabiting higher altitudes as increasing global temperatures bring new habitats into their range of tolerance, which might explain predictions of contracted areas of disease risk. In their previous study, members of the LIAM TBD group observed that risk of TBEV transmission in Hungary increased with warming temperatures. In their follow-up work, the effect on TBEV transmission was found to be linked to increases in several key parameters, such as increased duration of co-feeding between nymphs and larval ticks, and an increase in the duration of the 'questing' season.

To date, there is a lack of consensus on whether temperature or humidity itself, or the indirect effect of population density, has the greatest influence on actual range expansion. In the latter case, the effect could be self-limiting as

the environment becomes 'saturated'. Equally, counteractive human activities, such as decreasing populations of wild hosts through deforestation, or active use of pesticides, might modify the risk of TBE independently of climate change, albeit at greater expense. Overall, transmission risk of TBEV is predicted to increase between now and 2050 (at least in the Vas region of Hungary, a study area of the group), primarily because of the effect of warming temperatures on tick questing activity, the tick 'season', and co-feeding behaviours in tick lifestages.

Diseases such as Lyme disease, which have a reservoir in animal hosts, could be considered as more directly connected to variation in climate.

The public health expenditure necessary, either through education, vaccination, or more ecological interventions, will necessarily increase to restrain the risk of TBE in human populations under these conditions.



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Modelling of *Ixodes scapularis* populations across North America within the context of recent historical temperature changes suggests that the R_0 has increased directly in response to increasing temperature and is likely to continue this upward trend with future predictions of climate change. In some cases, the R_0 is expected to double from around 2-3 to as much as 7 in some areas over the next three decades. Populations where R_0 has changed from <1 to >1 also tended to coincide with newly established populations of ticks that have expanded from former ranges, carrying Lyme disease into areas where it did not exist before climatic changes made them conducive to tick survival. Clearly, the complexity of host-vector and vector-vector-host dynamics will play in an important part in the management of vector-borne diseases in a changing climate.

INFORMING OPTIMAL LOCALISED INTERVENTIONS

The research and knowledge mobilisation efforts by the LIAM TBD group based on their modelling framework have started to develop resources to assist others when incorporating co-feeding transmission into other vector disease modelling. These resources will be invaluable to researchers currently modelling the disease trends affected by vector-vector-host dynamics, as well as seasonal climate variations. Evidence is accumulating that climate change will increase the vector, host and pathogen reproductive capacity and, by extension, disease invasion and persistence for a variety of diseases such as malaria, dengue, Lyme disease and TBE. Whether these effects will be mitigated by more localised ecology, human activities and interventions, as we continually seek to manage and cultivate landscapes, and control pests and diseases through pesticides, vaccination programs, and health treatments is debatable, and will benefit from insights from modelling.

Behind the Research

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Research Objectives

The LIAM TBD working group has developed novel models incorporating non-systemic transmission to assess the risks of tick-borne disease outbreaks.

Detail

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Funding

The Canada Research Chairs Program, the National Science Foundation of China, and the Research project 'Estimating risk of tick-borne encephalitis with changes in climate, habitation and recreational activities', funded by GlaxoSmithKline SA.

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Personal Response

The LIAM TBD working group has followed a very logical series of modelling objectives to arrive at its current position – what are the next stages that will have the most impact?

Diapause – the delay in tick development in response to adverse environmental conditions – affects the co-occurrence of timing and clustering patterns of ticks in the hosts and thus modifies the co-feeding transmission efficiency to challenge tick-borne disease transmission risk assessment. An important next stage is to develop a comprehensive model incorporating diapause, co-feeding and systemic transmission, and using localised data to inform disease-risk spatiotemporal hotspots and interventions, including vaccine development and immunisation rollout. Equally important for the next stage modelling study is to incorporate prevention and control measures, such as deforestation and use of pesticides, to evaluate the cost-benefit of these measures, given the evolving knowledge of climate impact on diapause and co-feeding.

