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Linkages of Weather and Climate With *Ixodes scapularis* and *Ixodes pacificus* (Acari: Ixodidae), Enzootic Transmission of *Borrelia burgdorferi*, and Lyme Disease in North America

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Abstract

Lyme disease has increased both in incidence and geographic extent in the United States and Canada over the past two decades. One of the underlying causes is changes during the same time period in the distribution and abundance of the primary vectors: *Ixodes scapularis* Say and *Ixodes pacificus* Cooley and Kohls in eastern and western North America, respectively. Aside from short periods of time when they are feeding on hosts, these ticks exist in the environment where temperature and relative humidity directly affect their development, survival, and host-seeking behavior. Other important factors that strongly influence tick abundance as well as the proportion of ticks infected with the Lyme disease spirochete, *Borrelia burgdorferi*, include the abundance of hosts for the ticks and the capacity of tick hosts to serve as *B. burgdorferi* reservoirs. Here, we explore the linkages between climate variation and: 1) duration of the seasonal period and the timing of peak activity; 2) geographic tick distributions and local abundance; 3) enzootic *B. burgdorferi* transmission cycles; and 4) Lyme disease cases. We conclude that meteorological variables are most influential in determining host-seeking phenology and development, but, while remaining important cofactors, additional variables become critical when exploring geographic distribution and local abundance of ticks, enzootic transmission of *B. burgdorferi*, and Lyme disease case occurrence. Finally, we review climate change-driven projections for future impact on vector ticks and Lyme disease and discuss knowledge gaps and research needs.

Keywords

Lyme disease; climate change; Ixodes pacificus; Ixodes scapularis; Borrelia burgdorferi

The blacklegged tick, *Ixodes scapularis* Say,. is the primary vector to humans of a wide range of pathogens in the eastern United States and southeastern Canada. These include, but are not limited to, bacterial agents of Lyme disease (*Borrelia burgdorferi* sensu stricto) and

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anaplasmosis (*Anaplasma phagocytophilum*), a parasite causing babesiosis (*Babesia microti*), and Powassan encephalitis virus (Dennis et al. 1998, Homer et al. 2000, Piesman and Gern 2004, Brown and Lane 2005, Ebel 2010). In the past two decades, we have seen increases in both the overall numbers of Lyme disease, anaplasmosis, and babesiosis cases, and the geographic ranges of disease-endemic areas (Bacon et al. 2008, Ogden et al. 2014, Kugeler et al. 2015, Mead 2015, Mead et al. 2015). In the far western United States and southwestern Canada, the closely related western blacklegged tick, *Ixodes pacificus* Cooley and Kohls, is the primary vector to humans of *B. burgdorferi* and *A. phagocytophilum*. Impacts of a changing climate on the geographic distribution, local abundance, and phenology (seasonal activity) of *I. scapularis* and *I. pacificus* therefore may have direct consequences for several tick-borne human diseases. To exemplify the effects of current and changing climatic conditions for *I. scapularis*- and *I. pacificus*-borne diseases, we will focus on Lyme disease, the most commonly reported vector-borne disease in the United States and Canada (Bacon et al. 2008, Mead 2015, Ogden et al. 2015).

Climate variation is expected to be strongly associated with tick phenology because tick activity and survival are inhibited below minimum temperature thresholds. As a result, the length of the season ticks seek hosts is determined in large part by ambient temperature. Linkages between climate variability and the geographic distribution or local abundance of ticks will also occur, but may be confounded by availability and abundance of hosts. For example, the emergence (or re-emergence) and geographic spread of *I. scapularis* in the northeastern United States during the 20th century is Published by Oxford University Press on behalf of Entomological Society of America 2015. This work is written by US Government employees and is in the public domain in the US. considered to have been driven in large part by anthropogenic landscape change (reforestation of farmland) resulting in dramatic recovery of populations of the white-tailed deer, *Odocoileus virginianus* (Zimmerman), which is a key host of adult *I. scapularis* (Spielman et al. 1985, Spielman 1994, Wood and Lafferty 2013).

The northern limit of the ticks' ranges has been attributed to either too few days during the warm part of the year with temperatures exceeding thresholds that allow for physiological processes to proceed, or to cold temperatures in the winter limiting survival (Estrada-Pena 2002, Brownstein et al. 2003, Diuk-Wasser et al. 2010, Ogden et al. 2014). Both ticks are also absent from much of the Great Plains and the Intermountain West, presumably due to conditions that are too dry for these ticks to thrive (Dennis et al. 1998). Within the geographic area where climate conditions allow for these tick species to establish, we expect stronger linkages of weather and climate with tick abundance near the margins of their range than in core distributional areas with optimal temperature and moisture conditions.

Linkages between climate variability and enzootic pathogen transmission intensity are further complicated by vector ticks feeding on a wide range of vertebrates, with highly variable potential to serve as pathogen reservoirs (Piesman and Gern 2004). In the case of reservoir capacity for *B. burgdorferi*, hosts for *I. scapularis* and *I. pacificus* range from spirochete refractory (some lizard species) to potentially contributing only via cofeeding infection among ticks feeding in close proximity on noninfectious animals (some ungulates) and to serving as *B. burgdorferi* reservoirs and infecting feeding ticks with low, moderate, or

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high efficiency (birds and small mammals; Giardina et al. 2000, LoGiudice et al. 2003, Salkeld and Lane 2010). The composition of local host communities therefore is a major determinant for enzootic *B. burgdorferi* transmission intensity and infection rates in host-seeking ticks.

An additional but key consideration in linkages between climate variability and Lyme disease is the role human behavior plays in varying exposure to infected ticks. Among the outcomes for which weather and climate linkages are explored here, those relating to human Lyme disease cases may have the least direct and possibly the most difficult to interpret associations due to a plethora of confounding factors. In the current paper, we explore the impact of climate variability on: 1) the seasonal period and the timing of peak activity; 2) geographic tick distributions and local abundance; 3) enzootic *B. burgdorferi* transmission cycles; and 4) Lyme disease cases. Thereafter, we address climate change-driven projections for future impact on ticks and Lyme disease and, finally, discuss knowledge gaps and research needs.

General Introduction to *I. scapularis* and *I. pacificus*

The closely related *I. scapularis* and *I. pacificus*, both members of the *Ixodes ricinus* (L.) species complex, are three-host ticks and can be characterized as nonnidicolous (openly host-seeking) and host generalists. Larvae and nymphs of *I. scapularis* and *I. pacificus* feed readily on a wide range of hosts, including lizards, birds, insectivores, rodents, lagomorphs, and ungulates (Giardina et al. 2000, Casher et al. 2002, LoGiudice et al. 2003, Eisen et al. 2004, Salkeld and Lane 2010). The adult stage is restricted to larger mammals, such as medium-sized carnivores and, especially, cervids. The most important hosts for adult *I. scapularis* and *I. pacificus* are the white-tailed deer and Columbian black-tailed deer (*Odocoileus hemionus columbianus* [Richardson]), respectively (Piesman et al. 1979, Martin et al. 1981, Furman and Loomis 1984).

The likelihood of human encounters with these ticks depends upon life stage-specific host-seeking behavior and seasonality. In the Northeast, Upper Midwest, and southeastern Canada, all active stages of *I. scapularis* seek hosts during the warm part of the year (Piesman et al. 1987; Lindsay et al. 1999a, b; Gatewood et al. 2009; Hamer et al. 2012). All life stages ascend vegetation while seeking hosts, and therefore can be encountered by humans from a variety of substrates ranging from leaf litter to emergent grass and herbs. Host-seeking behavior is more multifaceted for *I. scapularis* in the southern reaches of its range and for *I. pacificus* in the far western states and provinces. In the southeastern United States, *I. scapularis* immatures rarely seek hosts openly from emergent vegetation and human contact therefore is primarily with the adult stage (Diuk-Wasser et al. 2006, Goddard and Piesman 2006, Stromdahl and Hickling 2012). The adult stage of *I. pacificus* is active from late fall to early spring, the wet part of the year along the Pacific Coast, and seeks hosts openly from grass, herbs, and brush (Lane 1990). Larvae and nymphs are active under drier conditions in spring and early summer (Eisen et al. 2001, 2002) and therefore more restricted in their host-seeking habits. Because they rarely ascend emergent vegetation, contact with humans occurs primarily in habitats with leaf litter free of emergent vegetation or from logs or tree trunks (Talleklint-Eisen and Lane 2000, Lane et al. 2007).

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Under optimal temperature conditions in the laboratory, the life cycles of *I. scapularis* and *I. pacificus* can be completed in <230 d (Troughton and Levin 2007). In the field, slower developmental processes, time spent to acquire bloodmeal hosts, and quiescence and diapause during parts of the year with unfavorable conditions lead to multiyear life cycles. The term diapause is frequently used to define any kind of delay in host-seeking activity or development. However, here we define diapause in ticks as a genetic trait for an arrest of development or activity arising from internal programing of the tick, which is usually switched on by and/or switched off by factors such as day-length, that may have evolved because they signal approaching unfavorable conditions. Ticks are inactive or arrest their development due to direct impacts of adverse environmental conditions (temperature or humidity) on metabolic processes of the tick, but this is perhaps best termed quiescence (Belozerov 2008). In addition to quiescence in host-seeking activity due to adverse temperature (too cold or hot) or low humidity (too dry) and slow development (too cold) that impact the life cycles of all ixodid ticks, two types of (mostly) weather-independent diapause may occur: 1) behavioral diapause, in which unfed ticks delay host-seeking activity even though weather conditions may be favorable; and 2) developmental (morphogenetic) diapause, in which eggs or fed immatures delay their development and fed mated females do not oviposit until many months after feeding, periods of time that are additional to that induced by effects of temperature on development rates (Oliver 1989, Sonenshine 1993). Therefore, the length and timing of the life cycle can be impacted by both ambient temperature-dependent quiescence of activity and development and temperature-independent, day-length-induced behavioral or developmental diapause. The interplay between temperature-dependent mechanisms and temperature-independent diapause inducement and termination drivers remain to be fully deduced for *I. scapularis* across its extensive geographic range (Sonenshine 1993, Belozerov et al. 2002, Belozerov and Naumov 2002, Ogden et al. 2004). The fact that this tick is successfully established in areas with a very wide range of local climates—from Florida to southeastern Canada—raises the possibility that plasticity in temperature-dependent and independent determinants of the life cycle phenology may be present. The length of the life cycle for *I. scapularis* ranges from 2 to 3–4 yr across its geographical range (Yuval and Spielman 1990, Lindsay et al. 1998, Hamer et al. 2012). For *I. pacificus* in northern California, Padgett and Lane (2001) described a 3-yr life cycle.

Climate Variation Linkages With Tick Survival and the Length and Timing of the Tick Life Cycle

Factors Affecting Mortality Rates

Host-seeking, engorged, and developing ticks suffer daily per-capita mortality in the field, so the ticks in any one particular life stage decrease in their numbers over time. This seasonal decay in tick abundance can generally be described by a simple negative exponential function; however, the fit to this function is not perfect and the observed variation is attributable to temperature and relative humidity (Vail and Smith 1998, Ogden et al. 2004). Ticks spend most of their lives off the host, so mortality rates in their environment can have a large impact on whether and where ticks can establish local populations, and if they do become established, how abundant they can become in a given area. Specific causes of

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mortality include: 1) freezing in the winter; 2) dehydration in dry spells in the summer; 3) overheating in summer; 4) drowning in flood water at any time of year; and 5) exhaustion of energy reserves in host-seeking ticks due to failure to find a host.

Ixodes scapularis has some resistance to short periods of cold conditions. Fed larvae and fed and unfed nymphs display low mortality when exposed to −10°C for 8 h, and the estimated temperature at which 50% mortality occurred for an 8-h exposure was −10.8°C for fed larvae, −16.4°C for unfed nymphs, and −11.6°C for fed nymphs (Vandyk et al. 1996). Exposure to lower temperatures and to subzero temperatures for longer periods produces almost universal mortality (Lindsay et al. 1995, Vandyk et al. 1996). Cold subzero temperatures experienced above ground in the northern parts of the *I. scapularis* range in winter would rapidly kill *I. scapularis* ticks in vitro (Vandyk et al. 1996). However in the field, in suitable woodland habitats, daily per-capita mortality in winter and summer is similar (Lindsay et al. 1995, Brunner et al. 2012), presumably because in the duff or surface layer of soil where the ticks seek refuge temperatures do not fall far below zero even if air temperatures fall below −30°C as they do frequently in Canada where *I. scapularis* is successfully invading (Ogden et al. 2009). Moreover, snow cover will further insulate ticks from low air temperatures, and it appears likely that mortality would result primarily from conditions that combine lack of snow cover with low air temperatures or repeated freezing and thawing of the ground substrate.

Typically, at very high temperatures ticks die because of water loss due to damage to the integument. The critical temperature for this to occur has been suggested to be as low as 32°C for *I. ricinus* but is above 40°C for other ixodid ticks (Balashov 1972, Sonenshine 1991). High temperatures (above circa 30°C) increase mortality rates (Ogden et al. 2004) and reduce oviposition success (Needham and Teel 1991) of *I. scapularis*. High temperatures also inhibit host-seeking activity (Vail and Smith 1998), which could indirectly increase tick mortality rates by reducing host finding success before the tick's finite energy resources are exhausted.

Within temperature thresholds for survival, tick survival rates are positively related with humidity (Schulze et al. 1986; Yuval and Spielman 1990; Needham and Teel 1991; Stafford 1994; Lane et al. 1995; Bertrand and Wilson 1996; Mount et al. 1997; Vail and Smith 1998; Eisen et al. 2002, 2003; Perret et al. 2003; Gray et al. 2009). Low humidity is lethal for ticks, and they need refugia in which they can re-hydrate. Low humidity also can have indirect effects on survival by forcing questing ticks to return more frequently to the duff layer to rehydrate, which depletes their finite energy resources and reduces the likelihood that they find a host before dying of starvation.

Factors Affecting Development Rates and Life Cycle Length—*I. scapularis*

Yuval and Spielman (1990) described a generalized 2-yr life cycle for *I. scapularis* in the northeastern United States. The female mates and feeds in the fall (Year 0) before entering developmental diapause over the winter (although some feed and then lay a single egg batch in the spring: Year 1). The larva hatches in the summer (Year 1), feeds, molts to the nymphal stage, and then enters behavioral diapause over the winter before seeking a host in the late spring and early summer of the following year (Year 2). The fed nymph molts to the adult

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stage in the summer (Year 2) and seeks a bloodmeal in the fall of the same year (Year 2). Key features allowing for completion of the life cycle in 2 yr in Massachusetts include: 1) fed larvae molting in the same year if they take their bloodmeal before September, leading commonly to overwintering of unfed nymphs; 2) fed nymphs molting in the same year if they take their bloodmeal before August; and 3) a warm season that is long enough for overwintered nymphs to feed in late spring, molt in the summer, and then feed again as females in the fall (Yuval and Spielman 1990).

It is clear, however, that in colder parts of the tick's range in southeastern Canada (Lindsay et al. 1995, 1998; Ogden et al. 2004) and the Upper Midwest of the United States (Hamer et al. 2012), the life cycle of some ticks in the population may be 3–4 yr in length. This likely occurs because: 1) fewer larvae feed successfully during the short late summer–early autumn activity period and overwinter unfed to quest the following spring (Lindsay et al. 1998); 2) more larvae that do feed in late summer–early autumn fail to molt before the onset of winter, resulting in more nymphs becoming active later in the following year; and 3) this delayed development, as well as later onset of questing nymphal activity due to cool spring temperatures, means that more nymphs feed after the summer solstice when day length is declining, and these fed nymphs then undergo developmental diapause over the winter to resume their development in the spring, not seeking hosts in the subsequent adult stage until the fall when cooler temperature favor activity (Duffy and Campbell 1994, Lindsay et al. 1998, Ogden et al. 2004).

Development rates are nonlinearly and positively related to temperature for each developmental stage (preoviposition period of engorged adult females, egg-to-larva development, engorged larva-to-nymph development, and engorged nymph-to-adult development), with development being likely zero at 0°C and fastest at >25°C (Ogden et al. 2004). This means that the length of the life cycle in large part is determined by how long temperatures are above the minimum temperature thresholds for development and activity of the different life stages, and how high above these thresholds temperatures reach, over the whole multiyear tick life cycle. Ogden et al. (2006) found the annual cumulative number of degree-days >0°C to be a convenient measure of annual cumulative temperature relevant to the duration of the tick life cycle. Temperature affects the duration of the life cycle, which in turn influences the survival of *I. scapularis* populations: the lower the temperature, the longer the life cycle and, given daily mortality rates, the less likely a larval tick is to survive to become a mated engorged adult female. In short, in colder climates the life cycle is prolonged, resulting in a lower basic reproductive number of *I. scapularis* (R_0: a metric of the capacity of the tick to reproduce given particular environmental conditions; Ogden et al. 2014) and a lower density of ticks (assuming similar densities of hosts for all tick life stages). Likewise, in warmer climates the life cycle is accelerated, resulting in a higher reproductive rate. However, eventually tick density will be regulated by high temperatures causing mortality and possibly also by density-dependent mechanisms, which may include the efficiency of grooming by hosts (Levin and Fish 1998) or acquired host immune resistance (Wilson et al. 1990, Craig et al. 1996).

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Factors Affecting Development Rates and Life Cycle Length—*I. pacificus*

The full life cycle of *I. pacificus* in northern California is considered to take 3 yr (Padgett and Lane 2001). Fed females oviposit from late winter to early spring (Year 0) and eggs hatch in mid- to late summer (Year 0). The larva then enters behavioral diapause until the following spring before seeking a bloodmeal host (Year 1). The fed larva molts in summer and the nymph, in turn, enters a behavioral diapause until the following spring before seeking a bloodmeal host (Year 2). The fed nymph molts to the adult stage in the summer (Year 2) and then seeks a bloodmeal in the winter of the following year (Year 3). The life cycle of *I. pacificus*, as described from northwestern California, is adapted to the climate in the far west, with hot and dry summers and cool and wet winters, by: 1) the host-seeking adults being active during the cool and wet winter months; 2) the immatures being active primarily in spring to avoid hot and dry summer conditions; and 3) the immatures host-seeking at the substrate surface only in protected habitats such as dense woodlands with leaf litter and not in open habitats such as grassland.

Climate Variation Linkages With the Seasonal Pattern of Questing Activity by Nymphs

The nymphal stage of *I. scapularis* and *I. pacificus* are considered the primary vectors of *B. burgdorferi* to humans (Spielman et al. 1985; Piesman et al. 1987; Clover and Lane 1995; Falco et al. 1996, 1999). We, therefore, focus on climate variation linkages with the seasonal pattern of questing activity by the nymphal life stage of these ticks.

Observed Seasonality of Host-Seeking in *I. scapularis* and *I. pacificus* Nymphs

The phenology of *I. scapularis* nymphs is similar across the northern parts of the tick’s geographic range in the United States and Canada. Nymphs become active in late March, peak from late May to early July, and then decline through October (Piesman et al. 1979, 1987; Wilson and Spielman 1985; Schulze et al. 1986; Lord 1995; Sonenshine et al. 1995; Ostfeld et al. 1996; Gatewood et al. 2009; Hamer et al. 2012; Orr et al. 2013). In southeastern Canada, and perhaps also in the extreme northern portions of the Northeast or Upper Midwest, activity of nymphs may start and peak slightly later, and end slightly earlier, than in most areas of the northeastern or midwestern United States (Lindsay et al. 1999a, Bouchard et al. 2011). Larvae that feed in the spring, rather than during the summer peak for larval activity, contribute to the late summer and autumn tail of the nymphal activity period (Lindsay et al. 1999a).

In the southeastern United States, *I. scapularis* nymphs are less likely to quest openly and studies on host-seeking ticks have yielded too few nymphs to be informative with regards to phenology (Cilek and Olson 2000, Diuk-Wasser et al. 2006, Goddard and Piesman 2006, Goltz and Goddard 2013, Gleim et al. 2014). Early studies based on museum lizard specimens or field-collected lizards showed that nymphs can be collected from lizards in the Southeast from March–September (Rogers 1953, Apperson et al. 1993, Oliver et al. 1993, Lavender and Oliver 1996), but most commonly from April–May (Oliver et al. 1993).

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The impact of weather on the phenology of *I. pacificus* nymphs was examined in north coastal California using nymphal abundance data collected over 4 yr in dry oak woodland sites and in a single year in a cooler and more humid and rainy redwood-tanoak site (Eisen et al. 2002). In the warm and dry oak woodland sites, nymphs were active by mid-March, reached 50% of their annual peak abundance in early mid-April, peaked by early May, fell below 50% of their observed peak abundance by early to mid-June, and were absent by late July to mid-August. The duration of time that nymphal abundance exceeded 50 or 75% of the observed peak was associated positively with rainfall and negatively with maximum air temperature during April–May. Compared with these oak-woodland sites, ticks collected from cooler-moister redwood sites typically reached 50% of their peak 10–15 d later, remained at levels above 50% of the peak 1.3–1.5 times longer, and started declining 4–6 wk later. Similar trends were also observed by Eisen et al. (2003). In general, compared with cooler coniferous areas, tick populations from warm and dry oak woodlands were characterized by a shorter duration of the total and peak nymphal questing season, an earlier nymphal peak, and a faster decline after the peak. Combined, these studies (Eisen et al. 2002, 2003) indicate that the density of *I. pacificus* nymphs consistently begins to decline between 21 and 23°C and when mean maximum daily relative humidity decreases below 83–85%.

Inducement of *I. scapularis* Nymphal Host-Seeking Activity in the Spring and Summer and Termination of Nymphal Host-Seeking Activity in the Summer and Fall

Laboratory studies indicate that temperature determines whether or not, and to what extent, *I. scapularis* can move to seek hosts, whereas humidity determines how high ticks quest above ground level, where their resource for re-hydration exists, and for how long they can remain actively host-seeking before retreating to re-hydrate (Clark 1995, Vail and Smith 1998, Ogden et al. 2004). Clark (1995) determined that the average temperature thresholds under which movement and coordinated movement by *I. scapularis* ceased were 9.8 and 13.9°C, respectively. However, some individual nymphs were capable of movement and coordinated movement at much lower temperatures, 4.2 and 6.3°C, respectively. Vail and Smith (1998) found no significant difference in the mean distance moved or time spent in questing posture for *I. scapularis* nymphs held at 10 versus 15 or 20°C, but observed that both movement and questing activity peaked at 25°C and fell sharply at 30°C. Therefore, the onset of activity in the spring by overwintering nymphs is likely associated (within any limits set by temperature-independent day-length-induced diapause) with key temperature thresholds being exceeded that allow for nymphs to move and seek hosts. Existing data are not adequate to pinpoint these thresholds, and additional studies focusing on temperatures in the 4–15°C range, using *I. scapularis* nymphs originating from different parts of its range, are warranted. Similarly, our understanding of the conditions that cause larvae having entered developmental diapause in the fall to resume development and molt to nymphs in the spring and summer requires further study.

The observed termination of nymphal host-seeking activity periods may be due to the effects of temperature (either becoming too cold or too hot for activity). However, host-seeking nymphal densities also decline as nymphs find bloodmeal hosts or through death from predation, parasitism, or exhaustion of energy reserves. The average life span in late spring

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and early summer for host-seeking nymphs in Westchester Co., NY, was estimated to be −25 d (Lord 1993). Observational and experimental studies also have shown that the longevity of host-seeking nymphs during the warm part of the year is negatively impacted by high temperatures and low humidity, particularly when relative humidity falls below 82% (Stafford 1994, Bertrand and Wilson 1997, Vail and Smith 1998, Rodgers et al. 2007, Berger et al. 2014a, Ginsberg et al. 2014). Further experimental studies, combined with field observations, are required to fully deduce what mechanisms are at play in determining *I. scapularis* seasonal activity patterns in different geographic regions.

Climate Variation Linkages With Interannual Variation in the Abundance of Host-Seeking Nymphs

Interannual variation in tick abundance is associated with variation in rainfall (particularly early-season drought) and cold winters, presumably via impacts on mortality rates of off-host ticks including questing nymphs (Jones and Kitron 2000, Berger et al. 2014b). However, such interannual variations in tick abundance also are strongly impacted by changes in abundance of key hosts for immatures (rodents) and adults (deer), which may or may not be related to weather conditions (Ostfeld et al. 2006, Simon et al. 2014). Contributing to our uncertainty in the effects of weather on interannual variation in tick abundance is limited data on: 1) mortality rates of each tick life stage related to weather effects at different times of the year; and 2) the shape and magnitude of the relationships between abundance of key hosts and abundance of host-seeking nymphs, particularly extended over multiple years. A contributing factor to uncertainty is that often useful local data for hosts of both immatures and adults, collected over a long enough period, are rarely available to parameterize predictive models, thus precluding robust forecasting the abundance of host-seeking nymphs.

Climate Variation Linkages With Spatial Occurrence of Ticks

Tick-borne pathogen transmission is limited to areas where vector ticks are present, so the most basic information needed to assess risk of human exposures is an accurate description of the geographic range of the vector tick species. Ticks require three conditions for their persistence: 1) a suitable climate for completion of their life cycle and host-seeking activity; 2) a suitable habitat that protects ticks from weather or other abiotic extremes that may kill them; and 3) suitable densities of host species from which to take bloodmeals. For *I. scapularis* there is evidence that populations at the northern limit of the range, and their rates of spread there, are limited by temperature in a way that has been predicted by simulation models of the effects of temperature on tick survival via effects on tick life cycle length (Ogden et al. 2006a,b, 2008a, 2014; Leighton et al. 2012; Bouchard et al. 2013b). To the west, low rainfall and humidity prevent *I. scapularis* from establishing in open prairie habitats, although they can persist in woodlands bordering on the prairie (Rydzewski et al. 2011, Rynkiewicz and Clay 2014) and perhaps along riparian corridors in prairie habitats.

Statistical models have identified climatic (temperature and relative humidity) determinants for *I. scapularis* distribution (Estrada-Pena 2002, Brownstein et al. 2003) and have produced broadly similar predicted geographic patterns of climatic suitability to that produced by

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simulation models (Ogden et al. 2006a, 2014). The statistical model of Brownstein et al. (2003) identified the negative effects of high temperatures on *I. scapularis* occurrence consistent with the laboratory observations cited above. These models also indicated a significant impact of humidity, but the relative importance and the variable representing humidity [e.g., vapor pressure variability: Brownstein et al. (2003) or the normalized difference vegetation index as a proxy for rainfall or relative humidity: Estrada-Pena (2002)] differed among the models. Strengthening support for the robustness of these predictors, another study developed based on systematic field sampling of *I. scapularis* (Diuk-Wasser et al. 2010) identified an elevation threshold above which no nymphs were found. Elevation is often a proxy for minimum temperature, which decreases with increasing altitude at a given latitude. Similar to the studies described above, humidity (measured as vapor pressure deficit) also had a significant impact on the tick's distribution.

Together these studies support the existence of a climatic envelope that delimits the possible geographic distribution of *I. scapularis*. However, within this climatically determined geographic frame, the actual presence and abundance of *I. scapularis* is determined by the existence of suitable woodland habitat and host densities. The emergence (or re-emergence) of *I. scapularis* in the late 20th century was likely driven by socioeconomic changes resulting in the migration of populations from rural regions into cities, abandonment of farms, and reforestation. These changes relatively rapidly reversed the deforestation and associated extirpation of white-tailed deer that had occurred gradually in the eastern United States throughout the post-Columbian era (Spielman et al. 1985, Spielman 1994, Wood and Lafferty 2013). Untangling this habitat–host dynamic from climate variation effects has proven difficult except at the very northern extent of the range where deer densities and habitat have been relatively stable during the period of recent northward *I. scapularis* spread (Leighton et al. 2012, Ogden et al. 2014).

The climate suitability envelope for *I. scapularis* is very large, operating at a subcontinental scale. Habitat suitability and host densities vary at a much more local scale, and studies conducted at State or sub-State levels frequently find that tick abundance and occurrence varies mostly with habitat, and climatic variables are weak predictors of tick abundance (Guerra et al. 2002, Khatchikian et al. 2012). Consistent with this, abundance of *I. scapularis* and *I. pacificus* can vary markedly over small geographic scales experiencing similar temperature and humidity conditions, further supporting the role of nonmeteorological factors, such as local host abundance, as important in determining local tick abundance (Eisen et al. 2003, 2010; Diuk-Wasser et al. 2006, 2010). Because of the strong confounding impact of host availability on tick population dynamics, climate variation associations are likely to be weaker predictors of tick abundance than tick presence or absence. This notion was supported in a modeling exercise for *I. scapularis* in the eastern United States (Diuk-Wasser et al. 2010, 2012) where a zero-inflated negative binomial model allowed for discrimination between variables predictive of presence or absence and those defining the density of host-seeking nymphs. Presence or absence was driven primarily by climatic variables and altitude, whereas nymphal density was primarily explained by the presence of host-seekig nymphs in neighboring sites.

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Enzootic *B. burgdorferi* Transmission in the United States and Canada

The typical cycle of *B. burgdorferi* transmission is for infected nymphal ticks to feed on and infect reservoir hosts, which then subsequently infect feeding larvae. The fed larvae maintain infection through the molt to infected and infective nymphs completing the cycle of transmission. For both *I. scapularis* and *I. pacificus*, transovarial transmission of *B. burgdorferi* either does not occur or is rare (Schoeler and Lane 1993, Rollend et al. 2013). The vast majority of immatures (larvae and nymphs) therefore can be assumed to acquire spirochetes while feeding on infectious reservoir hosts. Although the white-footed mouse, *Peromyscus leucopus* (Rafinesque), is considered to be the single most important source of *B. burgdorferi* infection for *I. scapularis* immatures, numerous other species of rodents, insectivores, lagomorphs, and birds may contribute locally as reservoirs (Levine et al. 1985, Donahue et al. 1987, Mather et al. 1989b, Giardina et al. 2000, LoGiudice et al. 2003). Deer do not contribute directly as *B. burgdorferi* reservoirs and may be zooprophylactic, with their innate immune system destroying *B. burgdorferi* in the gut of recently attached ticks that acquired infection either as larvae or nymphs (Telford et al. 1988, Ullmann et al. 2003, Bouchard et al. 2013a). The role of lizards and birds appears to vary with species. Not only are the key lizard hosts for *I. pacificus* immatures incompetent reservoirs for *B. burgdorferi*, but they also clear *Borrelia* from infected feeding ticks (Lane and Loye 1989, Lane and Quistad 1998, Giery and Ostfeld 2007). Some species such as skunks and raccoons may be inefficient reservoirs by virtue of being relatively resistant to infection, becoming immune rapidly and/or transmitting infection to few larvae (Fish and Daniels 1990, Norris et al. 1996). Eastern fence lizards (*Sceloporus undulates*) and five-lined skinks (*Eumeces fasciatus*) in the eastern United States are inefficient reservoirs either because they infect few ticks or because they carry few ticks even if they are capable of transmitting *B. burgdorferi* (Levin et al. 1996, Giery and Ostfeld 2007, Rulison et al. 2014). Birds vary widely in their competency as effective reservoir hosts (Mather et al. 1989a, Magnarelli et al. 1992, Ginsberg et al. 2005, Newman et al. 2015).

Climate Variation Linkages With Enzootic *B. burgdorferi* Transmission Intensity

In the previous sections we have focused on how climate variation impacts the occurrence and densities of ticks. Risk of human exposure to the Lyme disease spirochete depends on exposure to *B. burgdorferi*-infected ticks, particularly nymphs which are more likely than adult females to remain undiscovered and attached for long enough to transmit spirochetes. Acarological risk of exposure to *B. burgdorferi*-infected nymphs commonly is expressed as the density of infected nymphs (DIN). This risk measure is calculated as the product of the density of nymphs (DON) and their prevalence of *B. burgdorferi* infection (PIN). In the following, we assess evidence and predictions of the impact of weather or climate on PIN via impacts on *B. burgdorferi* transmission cycles. We assume that, by and large, greater abundance of vectors will result in more intense *B. burgdorferi* transmission cycles. Also it is recognized that in the southeastern United States, *I. scapularis* nymphs appear not to quest commonly above the duff layer and therefore are less likely to bite humans as compared with nymphs to the north (Diuk-Wasser et al. 2006, Stromdahl and Hickling 2012, Arsnoe et

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al. 2015). Apart from these factors climate variation can influence *B. burgdorferi* transmission cycles and PIN by: 1) affecting the abundance of reservoir hosts relative to the whole community of tick hosts; and 2) affecting the phenology of seasonal tick activity.

Occurrence and Relative Abundance of Reservoir Hosts of *B. burgdorferi*

A key determinant of the efficiency of *B. burgdorferi* transmission cycles is the proportions of tick hosts that are reservoir competent, relative to the proportion that are reservoir incompetent or even zooprophylactic. Subtle variations in host communities have been considered as being important in varying PIN in the northeastern and midwestern United States and southeastern Canada via the “dilution effect” whereby greater diversity of hosts results in greater proportions of ticks feeding on less efficient versus highly efficient (i.e. *Peromyscus leucopus*) reservoir hosts (LoGiudice et al. 2003, Ostfeld et al. 2006). To what extent host diversity impacts variation in DIN is not well studied, and some studies raise the possibility that reduced PIN is outweighed by greater DON with increasing biodiversity resulting in an “amplification effect”(Ogden and Tsao 2009, Swei et al. 2011). Broad changes in reservoir host communities in response to a changing climate may include: 1) host species changing their geographic ranges as appears to be the case in parts of southern Canada where *P. leucopus* mice are expanding their range northwards (Simon et al. 2014); and 2) effects of climate variability associated with climate change reducing biodiversity and increasing the proportions of ticks that feed on efficient hosts such as *P. leucopus* mice (Altizer et al. 2013).

Impact of Variation in Seasonal Tick Phenology on Enzootic *B. burgdorferi* Transmission

There is evidence for the impact of climate variation on the intensity of enzootic *B. burgdorferi* transmission via effects on the life stage-specific phenologies of infecting nymphal and infection-receiving larval *I. scapularis*. Transmission cycles would likely be most efficient if nymphs fed in advance of larvae allowing most infected hosts to pass any latent period and become infective by the time larvae feed (Spielman et al. 1985, Donahue et al. 1987). However, the earlier nymphs feed in the year before larvae, the more separated their peaks of activity become, and therefore the less efficient transmission may become due to the mortality of older infected animals before the larval peak occurs and the recruitment of noninfected juveniles that contribute to larval bloodmeals after the nymphal peak has passed. The least efficient transmission scenario is if the larvae feed earlier in the year than the nymphs.

Major reservoir hosts such as *Peromyscus* mice may have short lives and if seasonal asynchrony of nymphs and larvae is great, then fewer infected rodents may survive to infect larvae. Similarly if the duration of peak infectivity of reservoir hosts is short, transmission cycles will become less efficient as the duration of the seasonal asynchrony of nymphs and larvae increases. These factors have been combined in modelling studies to investigate potential effects of climate change on *I. scapularis*-borne pathogen transmission via effects on the seasonal phenology of immature ticks (Ogden et al. 2007, 2008a). By and large the predicted effects match observations made to date, with nymphal activity in spring and larval activity in summer as seen in the northeastern United States and southeastern Canada (Carey et al. 1981, Wilson and Spielman 1985, Schulze et al. 1986, Piesman et al. 1987, Lindsay et

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al. 1999a, Bouchard et al. 2011) resulting in moderately efficient transmission cycles (Ogden et al. 2008a). More synchronous activity of nymphal and larval *I. scapularis* in spring and summer in the Upper Midwest has been proposed to favor specific *B. burgdorferi* strains that produce short-lived transmittable infections in rodent reservoirs (Hanincova et al. 2008, Gatewood et al. 2009, Hamer et al. 2012). Synchronous seasonal activity of nymphs and larvae also is critical for transmission of infection between infected nymphs and uninfected larvae cofeeding on the same host, in the absence of systemic host infections [“cofeeding transmission” (Gern and Rais 1996)]. However, it is thought that this form of transmission plays a minor role in cycles of *B. burgdorferi* transmission in North America (Piesman and Happ 2001).

Warmer conditions in the Mid-Atlantic States may result in both spring nymphs and summer larvae becoming active earlier in the year [as seen in recent years in the northeastern United States: (Levi et al. 2015)] and some larvae molting into nymphs that are active in the fall of the same year. Even so the projected increase in the degree of synchrony of nymphal and larval activity was not great and increases in predicted intensity of pathogen transmission were small (Ogden et al. 2008a). In California, activity of *I. pacificus* larvae and nymphs is synchronous spanning early spring through to summer (Eisen et al. 2001), which would be expected to support efficient cycles of transmission were these not limited by the immature ticks feeding commonly on reservoir incompetent lizards and nymphal loads being low on rodent reservoirs (Eisen et al. 2004).

One notable caveat to this discussion of the impact of seasonal synchrony or asynchrony of nymphs and larvae on enzootic *B. burgdorferi* transmission intensity is that the actual loads of immatures on rodent reservoirs also will strongly impact local transmission intensity. A scenario in which degree of synchrony between nymphal and larval feeding is optimal but where infestation levels are low may result in less intense transmission than a scenario in which there is greater asynchrony between nymphal and larval feeding but much higher infestations of nymphs and larvae on rodent reservoirs (Ogden et al. 2008a).

Lyme Disease Incidence and Distribution in the United States and Canada

Since 1991, when standardized surveillance and reporting of Lyme disease began in the United States, case counts have increased steadily (Bacon et al. 2008, Mead 2015). Since 2008, >30,000 Lyme disease cases have been reported annually (Mead 2015). However, the geographic case distribution is very regional, cases occur seasonally, and interannual variation in case counts and seasonal onset is considerable (Bacon et al. 2008, Moore et al. 2014, Mead 2015). The two primary foci of Lyme disease in North America, with *I. scapularis* as the primary vector to humans, include: 1) the northeastern United States and southeastern Canada; and 2) the Upper Midwest of the United States and southern Manitoba and western Ontario. Another focus with far lower reported numbers of Lyme disease cases occurs in the far western United States and British Columbia in Canada, where *I. pacificus* is the primary vector to humans. Among and within these foci, incidence of Lyme disease cases follows spatio-temporal patterns mostly predictable by the known ecology of ticks and enzootic transmission cycles (Pepin et al. 2012).

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Throughout the United States, the majority of human cases report onset of clinical signs of infection during the months of June, July, and August, which is consistent with infections being acquired from nymphal ticks (Piesman 1989, Clover and Lane 1995, Bacon et al. 2008). During the period 1995–2013, the annual incidence of Lyme disease in the United States has increased steadily (Mead 2015). However, from 1992–2006, variation in case counts among years has been significant [up to 57%: Bacon et al. (2008)]. The start of the Lyme disease season, as measured by an increase in reported cases, differs by as much as 10 wk among the coolest and warmest Lyme disease endemic states in the eastern United States, and these differences have been linked to winter and spring climatic variability (Moore et al. 2014).

Climate Variation Linkages With Lyme Disease

Understanding when and where cases are most likely to occur is key to the efficient targeting of limited public health resources to times and places it will have most impact. The close correlation of geographic regions and seasons where DIN is known to be highest and the occurrence of Lyme disease cases in humans greatest (Pepin et al. 2012), underlines the close linkage of the biology of tick vectors and *B. burgdorferi* transmission in nature to where and when risk to the public occurs. As described above, the *B. burgdorferi* transmission cycle is complex and meteorological variables influence the components of the transmission cycle in varying ways together with the abundance of tick hosts and *B. burgdorferi* reservoirs. As a result, the impact of climatic variables becomes diluted or more difficult to discern when moving from timing of nymphal host seeking, to nymphal abundance, to DIN, to ultimately predicting when and where human Lyme disease cases are likely to occur. Compared with studies focusing exclusively on the tick or enzootic maintenance of *B. burgdorferi*, relatively few studies have evaluated the linkages between weather or climate and the spatial and temporal occurrence of human Lyme disease.

One study (Moore et al. 2014) sought to explore the timing of the start, peak, duration, and end of the Lyme disease season across 12 Lyme disease endemic states in the Northeast, Mid-Atlantic, and Upper Midwest. Across all 12 states and all years (1992–2007), the beginning of the Lyme disease season ranged from week 16 to 26 of the calendar year. However, 60% of the variation was attributable to the geographic variability of climatic and other environmental factors. Specifically, the Lyme disease season began earlier in warmer states that were more southern and coastal compared with cooler inland and northern sites. Consistent with findings that the onset of nymphal activity is positively associated with temperature (reviewed above), timing of the beginning of the Lyme disease season was strongly associated with cumulative growing degree days through week 20 of the calendar year. Cumulative growing degree days for a similar time period were also the strongest predictors of the peak and duration of the Lyme disease transmission season. This finding was consistent with the observation by Diuk-Wasser et al. (2006) showing that the peak of host seeking of ticks commenced earlier in the warmer southern states than in northern states. By contrast, the timing of the end of the Lyme disease season was not predicted by meteorological variables. This may be because the end of the season occurs when contact rates between humans and nymphs diminishes below some currently undefined threshold; this may be influenced not only by a decline in host-seeking nymphal density, but also

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seasonal changes in the duration of time humans spend outdoors. Although high temperatures are likely to cause significant tick mortality resulting in lower abundance of host-seeking nymphs, nymphal density is also reduced as a result of finding hosts (i.e., they are all bloodfed). Thus, host abundance, which was not included in these models, likely influences the timing of the end of the Lyme disease season.

Studies exploring geographical variation in Lyme disease case counts or incidence in the eastern United States have not shown clear or consistent associations with temperature or moisture (Ashley and Meentemeyer 2004, Tran and Waller 2013, Tuite et al. 2013, Robinson et al. 2015). Inconsistencies across studies could relate to differences in methodology and spatial scales. Variables other than climate may be more significant in predicting Lyme disease occurrence, particularly within the core distribution of the Lyme disease spirochete where variables such as host composition might be more important. However, temperature appears to be a driving factor in Lyme disease emergence at the northern limits of the current distribution where increasing temperatures favor the establishment of vector populations and increase the force of enzootic transmission of *B. burgdorferi* (Ogden et al. 2014, Robinson et al. 2015).

A limited number of studies have explored the association between weather and interannual variation in Lyme disease incidence. In these studies, precipitation emerged as a more significant predictor than temperature (Subak 2003, McCabe and Bunnell 2004). However, the mechanism by which precipitation influences human case occurrence remains unclear. In one study (Subak 2003), precipitation was measured with a 2-yr lag, in another study (McCabe and Bunnell 2004) there was merely a seasonal lag, suggesting inconsistent impacts of rainfall on the tick's life cycle.

Projected Effects of Climate Change on Tick Vectors, *B. burgdorferi* Transmission, and Lyme Disease

It is projected that climate will change in North America in the coming century (albeit with considerable geographic variation), and there is evidence that the climate has changed in recent decades. In general, both future projections and evidence to date indicate warming that increases in magnitude with latitude, increasing precipitation in the east and north east, and decreasing precipitation in the south and west (Intergovernmental Panel on Climate Change [IPCC] 2014). In addition, increasing climate variability and extreme weather events are projected and have been observed in recent decades (IPCC 2014). There are inherent uncertainties in all of the component parts of assessing future changes to Lyme disease risk which include: 1) how climate and weather impact Lyme disease risk (as reviewed above); 2) variations in projected climate produced by different global and regional climate models; 3) innate uncertainties in modelling some aspects of how climate is driven by atmospheric greenhouse gas accumulations; and 4) what will happen to atmospheric greenhouse gas concentrations in the future (a function of socio-economic activity, human population size, and the degree to which fossil fuels are used or replaced as an energy source).

A limited number of studies to date have investigated possible recent and future effects of climate change on tick vectors, reservoir hosts, *B. burgdorferi* transmission cycles, and Lyme

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disease cases. Four studies, three using variants or output of the same simulation model (Ogden et al. 2006a, 2008a, 2014) and one based on statistical modelling (Brownstein et al. 2005), provided roughly similar predictions for significant northward range expansion with climate change. One suggested significant contraction of the tick's distribution is associated with high temperatures in states bordering the Gulf of Mexico (Brownstein et al. 2005). All of these have used mean monthly values for climate variables; however, weather variability and extreme weather events may have less of an effect on ticks compared to mosquito vectors because ticks undergo development in (or to return to) litter layer refugia where they are protected from extreme temperature and rainfall. Most of these studies used output from one or a small number of climate models, but concordant results from an assemblage of models in one study support their projections (Ogden et al. 2014).

There is evidence for northward expansion of *I. scapularis* in Canada (Ogden et al. 2008b, 2011; Leighton et al. 2012), which is associated with increasing Lyme disease cases (Ogden et al. 2015), evidence that new tick populations are becoming established in areas where temperature conditions are now more favorable (Ogden et al. 2008b, 2011; Leighton et al. 2012), and synchrony of the northward spread of *I. scapularis* in Canada with a period of climate warming (Ogden et al. 2014). A similar northward expansion has been reported for *I. ricinus* in Sweden over the last 30 yr (Jaenson et al. 2012). There is also evidence for northward spread of *P. leucopus* rodents in southeastern Canada, with possible consequences for transmission where *I. scapularis* ticks have become established (Simon et al. 2014). To date, however, none of the observed changes in risk of exposure to *I. scapularis* or *B. burgdorferi* can be conclusively linked to climate change even though this may be a very likely cause or cofactor.

Other studies have explored projected seasonal changes in nymphal host-seeking phenology (Ogden et al. 2008a, Levi et al. 2015) and Lyme disease onset week (Monaghan et al. 2015) in relation to temperature. Taking into account uncertainty based on climate projection models and emissions scenarios, Monaghan et al. (2015) projected that on average across Lyme disease endemic states in the United States, the Lyme disease season would begin approximately 0.7–1.9 wk earlier by 2065–2085. This finding was consistent with Levi et al. (2015) who predicted that the peak of nymphal activity in New York would advance by 8–11 d by the 2050s. Both studies were based on regression analysis and do not explore climate-driven changes on the complete life cycle of *I. scapularis*. Notably, increasingly warmer temperatures could lead to shifts in nymphal host seeking from spring to late summer (Ogden et al. 2008). If this is indeed observed, Lyme disease onset week could theoretically shift to later in the calendar year.

Knowledge Gaps and Research Needs

Specific knowledge gaps differ for *I. pacificus* and *I. scapularis*, as well as for the latter species in different parts of its geographic range. A key question for the extreme Northeast, Upper Midwest, and Southeastern Canada is to what extent climate warming will result in spread and increased abundance of *Peromyscus* mice, deer, and *I. scapularis*, thus potentially placing new human populations at risk as well as resulting in increased transmission intensity in areas where *B. burgdorferi* already is established. For northern regions in

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general, a better understanding is needed of the potential impact of climate warming on the lifecycle of *I. scapularis*, the timing and synchronization of larval and nymphal populations, and the impact this may have on enzootic maintenance of *B. burgdorferi* and other *I. scapularis*-transmitted agents. In the southeastern United States, climate warming potentially could result in contraction of the range of *I. scapularis* or reduced potential for population increase, changes in the host-seeking behavior of different life stages, or changes to the tick's life cycle including the seasonal activity patterns of the different life stages. This is the portion of the range for *I. scapularis* for which the impact of climate warming is least intuitively clear. For *I. pacificus*, perhaps the most important question is to what extent climate warming will impact the host-seeking behavior of nymphs and lead to decreased or increased human contact with nymphs across the spectrum of climates from southern California to the Pacific Northwest and southwestern Canada. This question is further complicated by the greater uncertainty in how climate warming may drive changes in regional precipitation patterns, which can strongly influence tick survival and questing behavior, particularly in warmer areas. One critical need is for long-term monitoring and studies in strategic locations to follow change and validate modeling predictions in coming decades. Adaptive capacity to potential climate change-related increases in risk for tick-borne illnesses will depend largely on the development and validation of effective prevention and control tools and methods, including but not limited to vaccines and integrated tick management strategies.

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