Ecology, 87(5), 2006, pp. 1215–1224

DYNAMICS AND MANAGEMENT OF INFECTIOUS DISEASE IN COLONIZING POPULATIONS

Shirli Bar-David,[1,3] James O. Lloyd-Smith,[1,4] and Wayne M. Getz[1,2]

[1]*Department of Environmental Science, Policy and Management, University of California, 201 Wellman Hall, Berkeley, California 94720-3112 USA*
[2]*Mammal Research Institute, Department of Zoology and Entomology, University of Pretoria, Pretoria, South Africa*

Abstract. The introduction of chronic, infectious diseases by colonizing populations (invasive or reintroduced) is a serious hazard in conservation biology, threatening the original host and other spillover species. Most research on spatial invasion of diseases has pertained to established host populations, either at steady state or fluctuating through time. Within a colonizing population, however, the spread of disease may be influenced by the expansion process of the population itself. Here we explore the simultaneous expansion of a colonizing population and a chronic, nonlethal disease introduced with it, describing basic patterns in homogeneous and structured landscapes and discussing implications for disease management.

We describe expected outcomes of such introductions for three qualitatively distinct cases, depending on the relative velocities at which the population and epidemic expand. (1) If transmissibility is low the disease cannot be sustained, although it may first expand its range somewhat around the point of introduction. (2) If transmissibility is moderate but the wavefront velocity for the population, v_p, is higher than that for the disease, v_d, the disease wave front lags behind that of the population. (3) A highly transmissible disease, with $v_d > v_p$, will invade sufficiently rapidly to track the spread of the host.

To test these elementary theoretical predictions, we simulated disease outbreaks in a spatially structured host population occupying a real landscape. We used a spatially explicit, individual-based model of Persian fallow deer (*Dama mesopotamica*) reintroduced in northern Israel, considering a hypothetical introduction of bovine tuberculosis. Basic patterns of disease expansion in this realistic setting were similar to our conceptual predictions for homogeneous landscapes. Landscape heterogeneity, however, induced the establishment of population activity centers and disease foci within them, leading to jagged wave fronts and causing local variation in the relative velocities at which the population and epidemic expanded.

Based on predictions from simple theory and simulations of managed outbreaks, we suggest that the relative velocities at which the population and epidemic expand have important implications for the impact of different management strategies. Recognizing which of our three general cases best describes a particular outbreak will aid in planning an efficient strategy to contain the disease.

Key words: bovine tuberculosis; chronic disease; colonizing populations; Dama mesopotamica; *infectious disease; invasive species; Israel; managed disease outbreak; reintroduction; Persian fallow deer; population expansion; spatially explicit model.*

Introduction

Most studies of the spatial dynamics of infectious disease have focused on established host populations (e.g., Getz et al. 2006), either at steady state or fluctuating through time. Within a colonizing host population (invasive or reintroduced), however, the spread of disease may be influenced by the expansion process of the population itself: dispersal from the introduction site, home range establishment, and the development of population activity centers. This work investigates the simultaneous expansion of a colonizing population and a disease introduced by that population, in both homogeneous and structured landscapes, and explores the implications of such scenarios for disease dynamics and management.

Colonization processes of species are receiving increasing attention. The spatial spread of invasive species has been the subject of much empirical and theoretical study, because of the profound effects of these species on human economic systems, ecosystem function, and biodiversity (Andow et al. 1990, With 2002, Hastings et al. 2005). Also, much effort has been invested to ensure the success of programs aimed at reintroducing endangered species into the wild (Griffith et al. 1989, Beck et al. 1994).

Manuscript received 12 July 2005; revised 11 November 2005; accepted 17 November 2005. Corresponding Editor (ad hoc): R. J. Hall.

[3] Present address: Institute of Evolution, Faculty of Sciences, University of Haifa, Haifa 31905 Israel. E-mail: shirlibd@research.haifa.ac.il

[4] Present address: Center for Infectious Disease Dynamics, Mueller Lab, Pennsylvania State University, University Park, Pennsylvania 16802 USA.

Introduction of chronic infectious disease by these colonizing populations poses an important threat to conservation biology, even if the disease has only a marginal impact on natural mortality, because of the colonizing population's potential to become a reservoir host for the disease in question (Dobson and Foufopoulos 2001). When infected species invade, the pathogens they carry may spread to other host species that have no evolved defenses (Lafferty and Gerber 2002, Prenter et al. 2004), leading to direct and indirect effects on these species and on ecosystem evolution in the long term (Scott 1988, Woodroffe 1999). Infectious disease might also pose a serious threat to the successful establishment of reintroduced populations (Viggers et al. 1993, Cunningham 1996). Thus, understanding disease spread in colonizing populations has important implications for species conservation and managing biodiversity.

Populations undergoing colonization present unique patterns of mixing and spatial spread (Nugent 1994, Sjöåen 1997, Dolev et al. 2002, With 2002). Colonization can arise from single or repeated introductions of the host species, followed by dispersal to areas not yet occupied. If the population has a positive intrinsic growth rate (r_p) in the new environment, as we assume throughout this paper, it can spread into the surrounding landscape in a wave-like fashion, with a characteristic wave-front velocity under certain circumstances (Mollison 1991, van den Bosch et al. 1992). Shigesada and Kawasaki (1997) classified the patterns of increase in the range distance during this expansion phase into three types: linear expansion of the occupied area at a constant rate, biphasic linear expansion, and exponential expansion. The spatial spread is affected by the interaction of landscape structure (the spatial distribution of suitable habitats and the variation found among them) with population characteristics such as growth rate and dispersal traits (Jules et al. 2002, With 2002).

Introduction of an infectious disease to an established host population follows a similar pattern. The disease has the potential to invade successfully only if the basic reproduction number, R_0, defined as the expected number of secondary cases produced by one infectious case in a wholly susceptible population, is greater than 1 (Hudson et al. 2001, Getz and Lloyd-Smith 2006). The subsequent spatial spread of infectious disease is influenced by landscape structure and characteristics of the disease and host, such as transmissibility, the density and distribution of susceptibles, dispersal traits, and host vigor (Tilman and Kareiva 1997, Hess et al. 2001, Jules et al. 2002).

In this study we integrate the spatial dynamics of population colonization and the spread of a chronic, nonlethal disease, by focusing on the simultaneous expansion processes: a disease invasion within a colonizing host population. The topic of disease propagation in a colonizing population has only recently been considered from a theoretical point of view: Hilker et al. (2005) present a thorough analytic treatment of the impact of a lethal disease on invasion dynamics of a host species, under the assumptions of homogeneous landscape, diffusive host movement, and a strong Allee effect in host demographics. Some parallels exist with reaction–diffusion models of spatial predator–prey dynamics (e.g., Murray 1993, Owen and Lewis 2001) and with biological control applications where invading pests are combated by deliberate release of predators or parasitoids (e.g., Fagan et al. 2002). Our current work complements these studies and is novel in several respects. We study a chronic, nonlethal disease introduced simultaneously with a colonizing host population, whereas earlier work has examined lethal diseases (or predators) whose introduction lags that of the host (or prey). We apply elementary theoretical ideas to delineate regimes of behavior for the system, then test these predictions using a complex, individual-based model in a realistic landscape. Furthermore, we consider measures to control the invading disease and how management policies should be influenced by the dynamics of the simultaneous invasions.

The outline of the paper is as follows. First we describe the expected outcome of simultaneous disease and host introductions, in homogeneous landscapes. We outline three qualitatively distinct regimes that depend on the relative velocities at which the population and epidemic expand, under scenarios of different disease transmissibility (these may represent uncertainty regarding a particular disease, or different diseases). To illustrate these scenarios in a realistic setting, we consider the potential spread of bovine tuberculosis (*Mycobacterium bovis*; BTB) in a reintroduced population of Persian fallow deer (*Dama mesopotamica*) in northern Israel (Bar-David et al. 2005*a*), using a spatially explicit, individual-based model. Through simulations of this model, we explore the dynamics of the simultaneous expansion of the deer population and BTB infection, with reference to the theoretical regimes and spatial patterning of the host population (Bar-David et al. 2005*a*). Finally, we investigate the implications of these findings for disease management, exploring the extent to which particular management strategies might contain the disease as a function of the relative velocities at which the population and epidemic expand.

Expected Outcomes for Disease in a Colonizing Host

Processes governing the spatial dynamics of host colonization of a landscape and disease invasion into an established host population have commonalities regarding criteria for invasion. Both host and disease invasions can succeed only if the processes involved have intrinsic potential for growth ($r_p > 0$ and $R_0 > 1$, respectively) in the new environment. Simple models predict that, in a homogeneous landscape, a population will expand outward with a radially symmetric wave front, with some characteristic velocity if the "dispersal kernel"

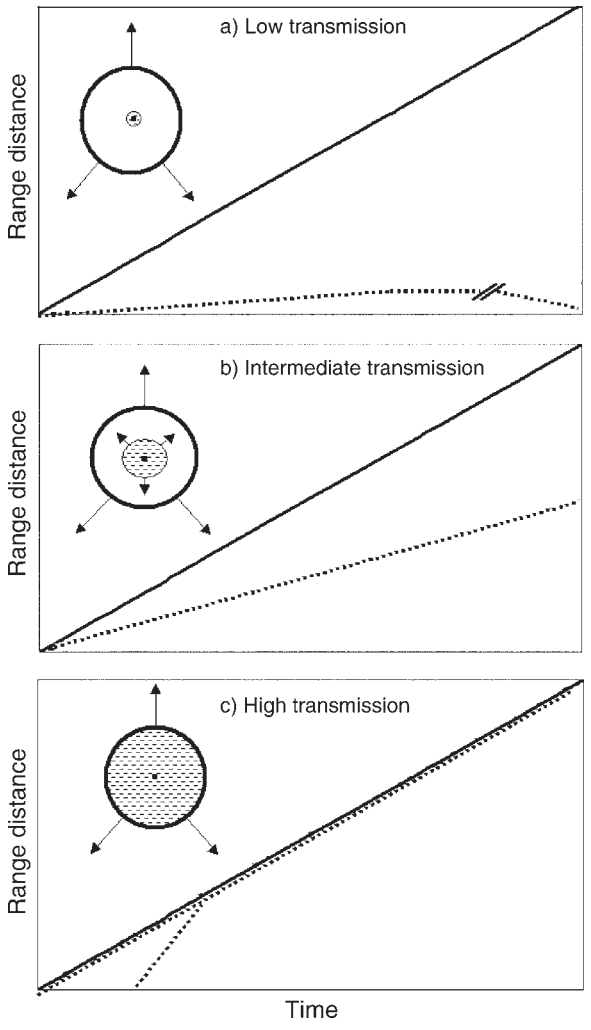

FIG. 1. Simultaneous invasion of host and disease: expectations in a homogeneous landscape. Shown is a schematic representation of range expansion vs. time for a colonizing host population (solid lines) and disease (dashed lines) for three ranges of disease transmissibility. Inset diagrams show spatial spread of the population (white area enclosed by heavy circle) and disease (stippled area) from the introduction site (black square), with arrows depicting the rate of expansion. Wave fronts of population and disease are assumed to advance with characteristic velocities v_p and v_d, respectively. Three scenarios of increasing transmission coefficients are depicted: (a) $R_0 < 1$, (b) $R_0 > 1$ and $v_d < v_p$, (c) $R_0 > 1$ and $v_d > v_p$. In panel (c), two disease range curves are shown, representing disease introduction at different times.

describing the distance of individual movements is exponentially bounded (Kot et al. 1996, Shigesada and Kawasaki 1997). Similarly, an introduced disease will expand spatially through the host population with a wave-front velocity that approaches a characteristic value if the "contact kernel" is exponentially bounded (Mollison 1991). The wave-front velocities for the host population (in a homogeneous landscape) and the disease (in an established host population), denoted v_p and v_d, respectively, can be characterized in terms of basic population and disease parameters in the context of simple models (Mollison 1991, van den Bosch et al. 1992, Hilker et al. 2005). Although details differ between models, the two velocities always increase with reproductive capacities (r_p and R_0 for v_p and v_d, respectively) and with some measure of host dispersal range.

Here we present a simple conceptual framework to describe the epidemiological and spatial dynamics when a chronic, nonlethal disease invades a colonizing host population. Similar delineations have been proposed before, in different contexts (Murray 1993, Owen and Lewis 2001, Hilker et al. 2005). The two expansion processes, occurring simultaneously, can interact in three qualitatively different ways (Fig. 1). If transmissibility is low, such that $R_0 < 1$, the disease cannot be sustained, although it may first cause a minor outbreak as a result of stochasticity in the infection process and, hence, expand its range somewhat around the point of introduction ("regime 1"; Fig. 1a). For a disease of moderate transmissibility, such that $R_0 > 1$ but $v_d < v_p$, the disease wave front may lag behind that of the host population, so there is an expanding annulus of uninfected hosts followed by a growing disease-affected core population ("regime 2"; Fig. 1b). This situation may persist until the population saturates the available habitat (e.g., on islands), after which the disease may eventually affect the whole population. A highly transmissible disease, with $R_0 \gg 1$ and $v_d > v_p$, may spread sufficiently rapidly to catch and track the spread of the host ("regime 3"; Fig. 1c). This can occur (after some delay) even if the spatial expansion of the disease begins after population expansion because, for instance, the disease is introduced later than the host, or the disease undergoes a period of stochastic stuttering before expansion.

This simple characterization will be influenced by the specific epidemiological details of real disease–host systems. For example, the average age at infection and average age at dispersal may interact significantly: disease spread will be slowed if most individuals disperse before becoming infected, or if individuals become infected and recover before dispersing. If the disease has a major detrimental impact on host fitness, it may reduce host range expansion due to individual lack of vigor or reduced population growth rates (Loehle 1995). In addition, disease may increase host movement due to specific symptoms or ejection from social groups due to dominance interactions (Bacon 1985, Loehle 1995). In the case of a lethal disease, if $v_d > v_p$, the host invasion front may be slowed down or reversed (possibly eradicating the host population), depending on the virulence of the disease (Hilker et al. 2005). If $v_d < v_p$, then a "doughnut effect" may arise whereby infectives near the introduction site die, but individuals that disperse outside the disease range continue to expand the host population. In our application, we focus on a chronic disease that has only a marginal impact on natural mortality, so we will not discuss the "highly

PLATE 1. Two females and fawn of Persian fallow deer (*Dama mesopotamica*). This endangered species is a subject of an ongoing reintroduction taking place in the Galilee, northern Israel. Photo credit: Eyal Bartov.

lethal" scenario further (but see Hilker et al. [2005]). In concluding this conceptual section, we note that a chronic, nonlethal disease in a colonizing host population can have important implications for the ecosystem it is invading: the colonizing species acts as a reservoir from which the disease can spread to other species that have no evolved defenses, where its effect could be lethal and could threaten the existence of those species (Dobson and Foufopoulos 2001).

IMPACTS OF LANDSCAPE AND POPULATION STRUCTURE

The population model

The possible outcomes just presented have the benefit of clarity, arising from assumptions of population and spatial homogeneity, but real outbreaks occur on spatially structured landscapes in populations that are heterogeneous with respect to movement behavior and disease dynamics. We can test our theoretical ideas in a more realistic setting using a model of an actual spatially structured host population colonizing a real landscape, where a credible threat of an introduced disease exists. We do this by extending an existing model of the spatial expansion of the reintroduced population of Persian fallow deer (*Dama mesopotamica*; see Plate 1) in northern Israel ("the deer model"; Bar-David et al. 2005*a*) to simulate a hypothetical outbreak of bovine tuberculosis (BTB, *Mycobacterium bovis*). The deer model has several important attributes for our exploration of simultaneous host and disease invasion: it is individual-based and stochastic, with detailed representation of home range establishment by individuals on a real landscape, and its predictions regarding deer range expansion have been validated using field-collected data (Bar-David et al. 2005*a*). Because the deer model was initially developed to address spatial–demographic questions, however, it includes only female deer. The relative importance of males for disease transmission in a colonizing population ultimately is unknown. Thus, these simulations are intended as an illustration of the types of phenomena that may be observed and as a tool for investigating the potential of various interventions for managing the disease.

The endangered Persian fallow deer has been reintroduced into northern Israel, with semiannual releases since 1996 (Saltz 1998, Dolev et al. 2002, Perelberg et al. 2003, Bar-David et al. 2005*b*). BTB has not been found in the Israeli deer population, but has been detected in European fallow deer (*Dama dama*), which appear to be a maintenance host for the disease (Morris et al. 1994, Mackintosh et al. 2004). BTB, a chronic, infectious disease known to easily invade long-lived social ungulates (Cross et al. 2005), is one of the most important pathogens of wild mammals worldwide (Morris et al. 1994). Introduction of BTB to an ecosystem by a colonizing population carries risks beyond the threat to the population itself (it has relatively minor effects on some reservoir species), and could have major impacts

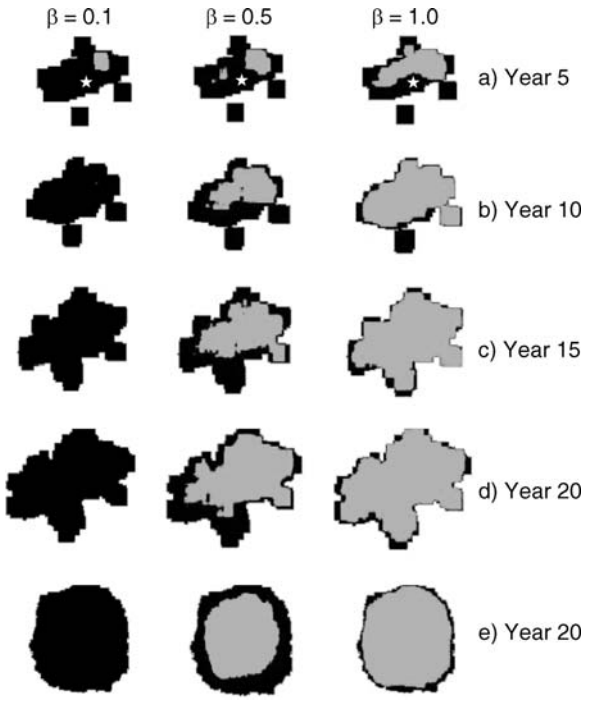

FIG. 2. Spatial expansion of simultaneously invading host population and disease. Range patterns are based on model projections to the end of 5, 10, 15, and 20 years since the onset of the reintroduction project of the Persian fallow deer, on the real landscape (a–d), and to the end of 20 years on an unstructured landscape (e), for three levels of disease transmissibility, β. Black denotes home ranges of all deer, and gray denotes home ranges of infected individuals; pixels were colored if the average number of individuals occupying them exceeded 0.5 over 250 runs. All simulations started with one infected individual among the first group released [release site in panel (a) indicated by a star]. Each pixel represents 100×100 m (total of 213×300 pixels).

through disease spillover to other hosts including humans and livestock (Bengis 1999). There is substantial incentive to contain BTB shortly after its introduction, because once established in wildlife reservoirs, it has proven exceedingly difficult to eradicate (Aranaz et al. 2004). This is particularly important in countries where eradication programs have substantially reduced the incidence of BTB, but sporadic outbreaks still occur (Caffrey 1994, Simpson 2002, Aranaz et al. 2004).

We describe the extended model briefly here, and give details in Appendix A. The model includes processes pertaining to the release, dispersal, home range establishment, survival, reproduction, and disease transmission of individual Persian fallow deer. The reintroduction program is modeled as annual release of female deer from a habituation enclosure (10 females/year for years 1–5, then 5 females/year for years 6–10; see Saltz [1998]). Dispersal and home range decisions are influenced by habitat quality, which is scored for 1-ha pixels over the study area (a 639-km^2 section of the Galilee region of Israel, between 32°54′ to 33°05′ N and 35°09′ to 35°28′ E). To distinguish the influence of landscape heterogeneity from other aspects of model structure, we also ran simulations on unstructured landscapes for which habitat quality scores were generated as independent, uniform random variants on the same range as the real scores. Survival and reproduction of deer are age-dependent, stochastic processes. We modeled the disease as an SEI (Susceptible, Exposed but not infectious, Infectious) process (Hudson et al. 2001), with epidemiological characteristics of BTB and no effect on host recruitment, behavior, or survival (McCarty and Miller 1998). We modeled disease transmission as a stochastic, spatially structured horizontal process, with density-independent contacts among deer proportional to the spatial overlap of individual home ranges as indicated in field studies (Perelberg 2000). For the transmission coefficient, β, we drew upon empirical estimates for farmed European fallow deer populations, which indicated that β could take values in the range 0.1–1 (Wahlström et al. 1998). Transmission between mother and calf could also occur with nonzero probability within the calf's first year of life (McCarty and Miller 1998).

Simulation results

Despite the introduction of host population structure and landscape heterogeneity, the three conceptualized regimes (Fig. 1a–c) are clearly evident in the simulated outbreaks (Figs. 2 and 3). As predicted, the relative rates of range expansion for the host population and for the chronic disease (introduced with the host population) were influenced considerably by the disease's transmissibility. Moreover, β values corresponding to the estimated range of BTB transmissibility in European fallow deer (Wahlström et al. 1998) led to simulated outbreaks spanning all three possible outcomes for the simultaneous invasion. At the low end of the estimated values ($\beta = 0.1$), the disease range initially expanded slightly, but ultimately decreased (Fig. 2). As transmissibility increased (e.g., $\beta = 0.5$), the disease took hold, but its wave front lagged behind the wave front of the host population (Fig. 2). At the high end of the estimated range ($\beta = 1$), the disease closely tracked the expanding host population (Fig. 2). However, although the range distance of the host population expanded in a biphasic pattern (a high linear rate in the first years, due to intensive releases, followed by a slower rate during subsequent years) the average disease range expanded at a constant velocity (Fig. 3). This is presumably because the velocity of the disease range expansion was not affected by released individuals that dispersed immediately from the introduction site and established home ranges beyond the frontier of the disease range.

Comparison of simulations on the real landscape vs. unstructured random landscapes reveals that landscape structure leads to jagged wave fronts (Fig. 2) and the establishment of population "activity centers" (concen-

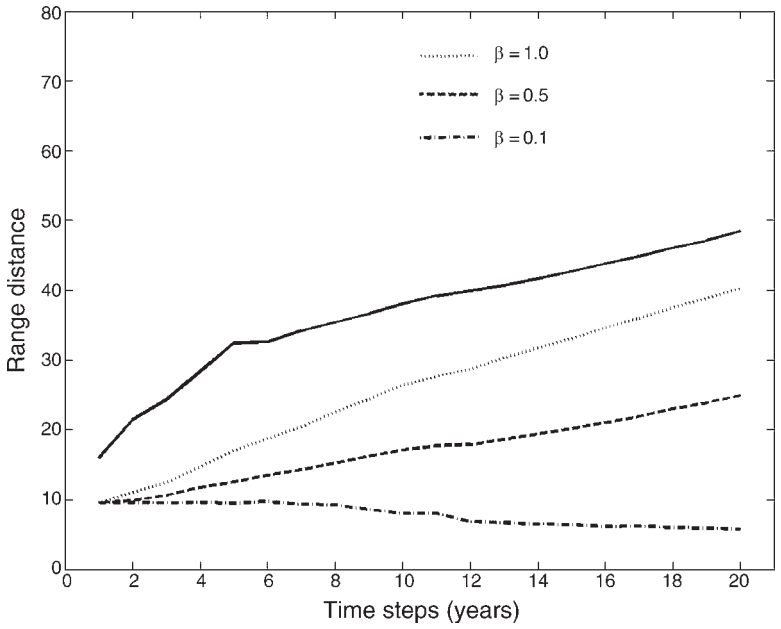

FIG. 3. Range distance of host population and disease. Model projections on the real landscape are plotted for 20 years from the onset of the reintroduction project of the Persian fallow deer: the solid line is the range distance of the deer population (average of five spatial scenarios); the broken lines are the range distance of the disease (average of 250 runs) under three different disease transmissibilities, β. All simulations start with one infected individual. The range distance was calculated as the square root of the area occupied divided by $\sqrt{\pi}$.

tration of deer in preferred habitats; Bar-David et al. [2005*a*]) and "disease centers" (relatively high concentration of infectives) within them (Fig. 4). As the transmissibility increased, the disease spread faster from the release site and disease centers developed even in more remote activity centers (Fig. 4). Landscape heterogeneity caused the relative velocities at which the population and the epidemic expanded (v_d/v_p) to vary between areas, differing from the ratio anticipated from simulations in the unstructured landscape. For instance, at the eastern boundary of the deer distribution, the disease wave front almost caught up with that of the population, even in the moderate transmissibility scenario ($\beta = 0.5$), whereas at the western boundary the disease lagged the population substantially (Fig. 2). The ratio v_d/v_p in the eastern zone was higher than in the western zone, apparently because settlements and low-quality habitat in the east inhibit the population expansion (akin to reaching the shore of an island). As a result, the overall outbreak appears as a combination of two regimes, "regime 3" in the east and "regime 2" in the west, induced by the effect of landscape heterogeneity on disease and host wave-front velocities.

In the preceding analyses, we focused on the average spatial extent of host population expansion and simultaneous disease invasion. Our results can also be integrated over space to show the total population dynamics, as well as the variation in outcome due to stochasticity (Appendix B). These results reemphasize that transmissibility values throughout the plausible, empirically determined range for BTB in fallow deer lead to highly disparate outcomes for disease invasion and persistence in a colonizing population. For low transmissibility ($\beta = 0.1$), the probability of disease extinction (p_{ext}) over the 20-year simulation was high, although the outbreak did persist due to stochasticity in some simulations (e.g., $1 - p_{ext} > 0.4$ after 10 years, $1 - p_{ext} > 0.15$ after 20 years). Moderately and highly transmissible diseases exhibit infrequent extinction and faster growth: for $\beta = 1$, the disease persisted for 20 years in more than 95% of simulations, with >50% of all females infected, on average (79 ± 32 out of 133 ± 25 individuals, mean ± SE).

Implications for Disease Management

Each of the three conceptual regimes (Fig. 1), verified as plausible scenarios in the context of BTB being introduced by a colonizing population of Persian fallow deer (Figs. 2 and 3) (and probably also relevant to other chronic diseases in other hosts), has its own implications for management strategies aimed at curtailing the establishment of a disease reservoir. Regime 1 is of minimal concern because the disease is likely to go extinct without intervention, although some management is suggested to minimize the possibility of spread to other species. If there is potential for disease establishment, however, we suggest that specific management strategies, along the lines that we will elaborate, should be applied depending on the regime (2 or 3) and the goals of management. When the disease wave front lags

behind that of the population (regime 2), then measures focused on the infected core of the population may ultimately prevent the disease from spreading to the outer disease free zone. When the disease wave front tracks the population closely (regime 3), then disease management measures should cover the entire range of the host. In both cases, the management goal can be to eradicate the disease or, sometimes more realistically, to establish disease-free subpopulations that can be isolated in some way, while containing the disease in areas where prevalence is high. In reintroduction programs, the possibility of stopping further releases because of impacts on population viability and on disease spread should be considered for each regime.

We explored disease management through simulation, using our extended deer model. We modified the model to evaluate the potential efficacy of the following four disease management strategies (for details, see Appendix C). In the first strategy, further releases of deer were halted once the outbreak was recognized. In the other three, vaccination was used to protect different groupings of released individuals and wild-born young (using an idealized vaccine, as discussed in Appendix C). All strategies were deployed from the third year after initial release onward (i.e., after 20 individuals have been released over the first two years), assuming a two-year delay to identify and respond to the disease in the wild population.

We found, on the basis of our model assumptions, that stopping further releases in the reintroduction program, even at an initial stage of the program, had minimal effect on eradication of a chronic disease of high-to-moderate infectiousness (regimes 2 and 3). The stop–release strategy raised the probability of disease extinction within 20 years by only 5–10% for any scenario (Appendix C), suggesting that additional management interventions are required. When animal releases were continued, varying degrees of control were achieved through vaccination (Appendix C). Spatially targeted vaccination (with efforts focused in a core region around the introduction site) appeared to be more effective than comparable levels of coverage through the entire population range, but this effect was most noticeable for the moderately transmissible disease (regime 2). For a highly infectious disease (regime 3), only a vaccination strategy with complete coverage of all wild-born and released individuals could cause a substantial increase in the probability of disease extinction within 20 years ($p_{ext} > 0.5$, Appendix C).

Broadscale disease management of wildlife populations presents considerable challenges (McCallum and Dobson 1995, Woodroffe 1999, Lafferty and Gerber 2002). Because conducting a specific management strategy (such as vaccination) throughout the entire range of an expanding population often will not be feasible, it is useful to assess reduced strategies. Based on our findings, we suggest that recognizing which of the regimes in Fig. 1 applies best to a given situation can aid

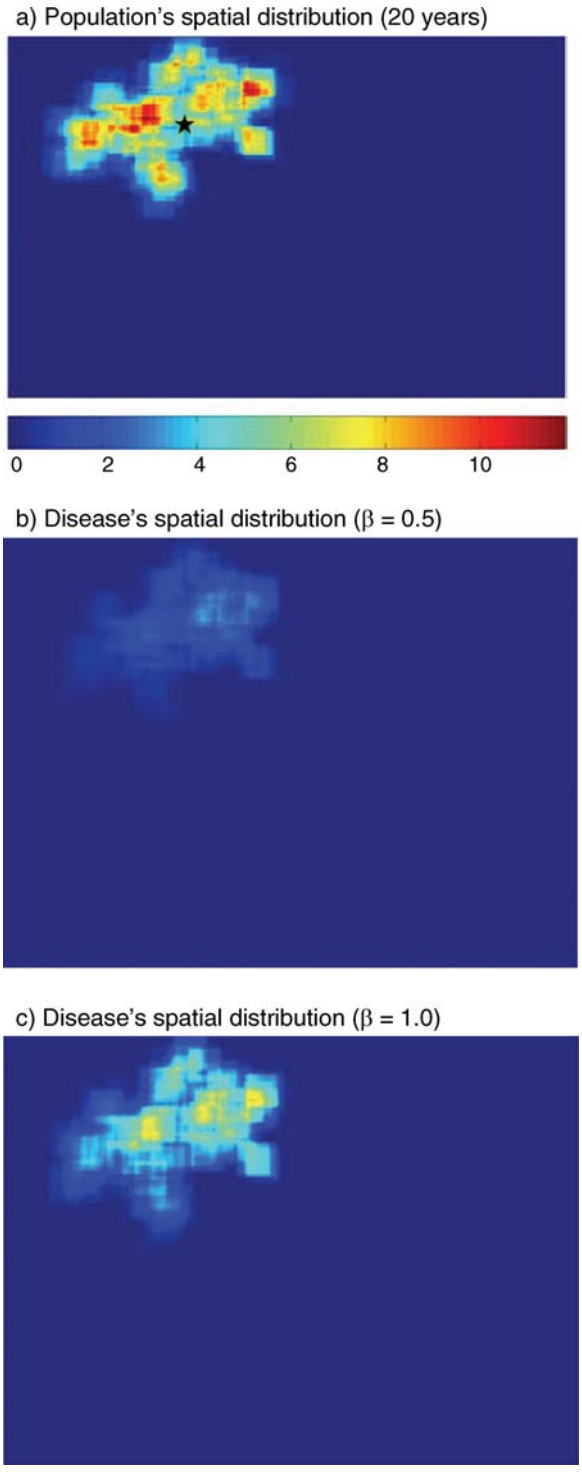

FIG. 4. Spatial distribution of host population and disease 20 years after colonization begins. The patterns are based on model projections: (a) spatial distribution of the deer population; (b) spatial distribution of the disease ($\beta = 0.5$); and (c) spatial distribution of the disease ($\beta = 1$). The color represents the average number of individual home ranges overlapping each pixel, for all deer (a) or only infected deer (b, c). Notice the population and disease activity centers: areas with high densities of individuals and infected individuals, respectively. Pixels represent 100×100 m (total of 213×300 pixels), and a star indicates the release site.

in designing the most efficient and feasible disease management strategy. Our conclusions regarding management should apply generally to chronic, nonlethal diseases affecting colonizing host populations, but may not hold for acute or lethal diseases. Future studies should examine the effectiveness of other strategies that may prevent further expansion of the disease (regime 2), thereby maintaining a disease-free portion of the population in the outer range. Such strategies could include fencing in the diseased population or applying vaccination or test-and-remove policies around the leading edge of the epidemic. Also, future studies could examine the effectiveness of concentrating intervention efforts in specific sites such as the introduction site or population activity centers that have the potential to develop into disease foci.

Discussion

Having argued for the importance and practical relevance of our three-regime framework (Fig. 1), it is worthwhile to consider how the applicable regime could be determined in a field situation. We suggest that disease prevalence be tested along transects radiating outward from the introduction site, to ascertain the relative positions of the disease and population wave fronts. It is crucial to conduct these tests along transects in several directions, because of possible landscape-driven variation in the relative velocity at which the population and disease expand (Fig. 2). In such settings, a combined approach using different regime-specific management strategies in different regions may be optimal.

We derived disease parameters for our model from data pertaining to BTB in captive populations of other deer species (McCarty and Miller 1998, Wahlström et al. 1998). Although the epidemiology of BTB in captive deer populations has received considerable scrutiny (e.g., Griffin and Mackintosh 2000, Mackintosh et al. 2004), little is known about the disease in free-ranging populations of deer (but see O'Brien et al. 2002). In wild deer, where the population density is low, reports indicate that BTB prevalence is lower than in captive deer populations (Wahlström et al. 1998). Hence, the transmission coefficients used in this work might be higher than in wild populations, offsetting to some extent the underestimation due to omitting males. Because males may play a major role in disease transmission (O'Brien et al. 2002), e.g., as mixing agents due to possible life-long movements, we expect our results to underestimate the effects of disease. Because the model describes a colonizing population, however, all individuals are mixing and dispersing due to the population expansion process, so we assume that the relative importance of males will be diminished compared with an established population where males account for most dispersal. Potential influences of disease on survival, reproduction, and movement patterns of infected individuals were not modeled, in keeping with reports of minor disease impacts for several ungulate maintenance hosts of BTB (McCarty and Miller 1998, Rodwell et al. 2001).

Directions for future work

Several avenues of future research would help to develop these ideas further. To explore the generality of our approach, models of invasive spread (preferably linking population spread to landscape structure, With 2002) can be adapted to explore disease dynamics in other case studies of real colonizing populations. Such models will also provide tools for evaluating further management alternatives, as we have suggested, thus improving our ability to respond to future disease outbreaks. Our findings should be generalized to include the male demographic component, transient diseases, and diseases that severely impact host survival (Hilker et al. 2005) or movement, either through further case studies or through theoretical investigations outlining dynamical regimes (Fig. 1). Recovery and disease-induced mortality both act to reduce the duration of the infectious period, and therefore can strongly influence disease invasion and persistence by altering the relative timescales of disease, demographic, and movement processes (Cross et al. 2005, Lloyd-Smith et al. 2005). If the diseases become established and form traveling waves, then the simple regimes that we have predicted may be altered. For a transient disease, from which the host can recover, the analogue of regime 2 may be an expanding, ring-like wave of disease, whereas the analogue of regime 3 might be a disease that overtakes the host wave front and goes extinct (essentially outpacing its fuel supply). Details will depend on the existence and duration of host immunity following recovery. For a lethal infectious disease, regimes 2 and 3 might correspond, respectively, to a wave of mortality lagging the population wave front and to complete extinction of the host. Also, as reported by Hilker et al. (2005), a deadly disease might slow down or reverse the invasion wave front of the host, when deaths due to infection overbalance the growth at the population front. Obviously, in such cases the disease would have great relevance to population viability in a reintroduction effort, or equivalently, would have great utility as a biological control agent.

The generality of our results with regard to the management of transient and lethal diseases needs to be assessed. The changes in basic disease–host dynamics, induced by changes in the relative timescales of disease and other processes, will interact with management strategies in ways that depend on the details of host mixing and movement. In particular, the greater efficacy of spatial vaccination policies focusing on the core region surrounding the introduction site will not hold when the disease range forms an expanding ring and halting further releases of susceptible hosts may have greater efficacy for diseases with shorter infectious periods.

Conclusions

Host populations undergoing colonization present unique patterns of mixing and spatial spread that may govern the dynamics of invasive spread of infectious diseases. Based on theoretical considerations in a homogeneous landscape, we outlined three qualitatively distinct regimes of expected behavior for a chronic, nonlethal disease introduced by a colonizing host (Fig. 1). These provided a canonical foundation for the range of patterns observed in our simulations of a hypothetical BTB epidemic in the Persian fallow deer population recently reintroduced in northern Israel (Fig. 1 vs. Fig. 3). These patterns could describe the likely spatial dynamics of other systems with chronic, nonlethal diseases infecting colonizing hosts. We found, however, that the heterogeneity of the realistic landscape induced the establishment of population activity centers in preferred habitats and the development of disease centers within them. Landscape heterogeneity also caused the relative velocities at which the population and epidemic expanded to vary among regions, sometimes leading to spatial mixtures of qualitative regimes for a given outbreak.

Within a range of disease transmissibility drawn from analysis of BTB in fallow deer, different β values led to simulated outbreaks spanning all three dynamical regimes for the simultaneous invasion. Thus we see that uncertainty regarding a disease's transmissibility, perhaps inevitable when considering a disease in a new host species or environment, can challenge our ability to assess the likelihood of long-term persistence and the rate of spread within a population, and hence the threat to other species in the ecosystem. We suggest that recognizing which of the regimes best describes a situation in the field can aid in planning disease management and in choosing the most efficient and feasible strategy.

There is an obvious difference between introduced (invasive) and reintroduced species in terms of conservation: management of introduced species focuses on their eradication and diseases can serve as biological control agents (Simberloff and Gibbons 2004), whereas for reintroduced species, conservation efforts seek to ensure persistence of the population and pathogens are a major threat. In both cases, though, the impact of a novel disease introduced to the ecosystem goes beyond the threat to a particular species. Thus, understanding disease invasion within an expanding population is an important basis for interpreting observed patterns and evaluating management strategies aiming to contain disease spread.

Acknowledgments

Grants to W. M. Getz from the NSF/NIH Ecology of Infectious Disease Program (DEB-0090323), NIH-NIDA (R01-DA10135), and the James S. McDonnell Foundation 21st Century Science Initiative supported this research. We are grateful for constructive discussion with Cherie Briggs and the comments on previous versions of this manuscript made by Maria S. Sanchez, Paul C. Cross, David Saltz, Allison L. Bidlack, Sadie J. Ryan, and Leo C. Polansky.

Literature Cited

Andow, D. A., P. M. Kareiva, S. A. Levin, and A. Okubo. 1990. Spread of invading organisms. Landscape Ecology **4**: 177–188.

Aranaz, A., et al. 2004. Bovine tuberculosis (*Mycobacterium bovis*) in wildlife in Spain. Journal of Clinical Microbiology **42**:2602–2608.

Bacon, P. J. 1985. Population dynamics of rabies in wildlife. Academic Press, New York, New York, USA.

Bar-David, S., D. Saltz, and T. Dayan. 2005*a*. Predicting the spatial dynamics of reintroduced populations: the Persian fallow deer. Ecological Applications **15**:1833–1846.

Bar-David, S., D. Saltz, T. Dayan, A. Perelberg, and A. Dolev. 2005*b*. Demographic models and reality in reintroductions: Persian fallow deer in Israel. Conservation Biology **19**:131–138.

Beck, B. B., L. G. Rapaport, M. R. S. Price, and A. C. Wilson. 1994. Reintroduction of captive-born animals. Pages 265–286 *in* P. J. S. Olney, G. M. Mace, and A. T. C. Feistener, editors. Creative conservation: interactive management of wild and captive animals. Chapman and Hall, New York, New York, USA.

Bengis, R. G. 1999. Tuberculosis in free-ranging mammals. Pages 101–114 *in* M. E. Fowler and R. E. Miller, editors. Zoo and wild animal medicine. W. B. Saunders, Philadelphia, Pennsylvania, USA.

Caffrey, J. P. 1994. Status of bovine tuberculosis eradication programs in Europe. Veterinary Microbiology **40**:1–4.

Cross, P. C., J. O. Lloyd-Smith, P. L. F. Johnson, and W. M. Getz. 2005. Duelling timescales of host movement and disease recovery determine invasion of disease in structured populations. Ecology Letters **8**:587–595.

Cunningham, A. A. 1996. Disease risks of wildlife translocations. Conservation Biology **10**:349–353.

Dobson, A., and J. Foufopoulos. 2001. Emerging infectious pathogens of wildlife. Philosophical Transactions of the Royal Society of London Series B, Biological Sciences **356**: 1001–1012.

Dolev, A., D. Saltz, S. Bar-David, and Y. Yom-Tov. 2002. Impact of repeated releases on space-use patterns of Persian fallow deer. Journal of Wildlife Management **66**:737–746.

Fagan, W. F., M. A. Lewis, M. G. Neubert, and P. van den Driessche. 2002. Invasion theory and biological control. Ecology Letters **5**:148–157.

Getz, W. M., and J. O. Lloyd-Smith. 2006. Basic methods for modeling the invasion and spread of contagious disease. *In* Z. Feng, U. Dieckmann, and S. A. Levin, editors. Disease evolution: models, concepts, and data analysis. American Mathematical Society, Providence, Rhode Island, USA, *in press*.

Getz, W. M., J. O. Lloyd-Smith, P. C. Cross, S. Bar-David, P. L. Johnson, T. C. Porco, and M. S. Sanchez. 2006. Modeling the invasion and spread of contagious disease in heterogeneous populations. *In* Z. Feng, U. Dieckmann, and S. A. Levin, editors. Disease evolution: models, concepts, and data analysis. AMS, *in press*.

Griffin, J. F. T., and C. G. Mackintosh. 2000. Tuberculosis in deer: perceptions, problems and progress. Veterinary Journal **160**:202–219.

Griffith, B., J. M. Scott, J. W. Carpenter, and C. Reed. 1989. Translocation as a species conservation tool: status and strategy. Science **245**:477–480.

Hastings, A., et al. 2005. The spatial spread of invasions: new developments in theory and evidence. Ecology Letters **8**:91–101.

Hess, G. R., S. E. Randolph, P. Arneberg, C. Chemini, C. Furlanello, J. Harwood, M. G. Roberts, and J. Swinton. 2001. Spatial aspects of disease dynamics. Pages 102–118 *in*

P. J. Hudson, A. Rizzoli, B. T. Grenfell, H. Heesterbeek, and A. P. Dobson, editors. The ecology of wildlife diseases. Oxford University Press, New York, New York, USA.

Hilker, F. M., M. A. Lewis, H. Seno, M. Langlais, and H. Malchow. 2005. Pathogens can slow down or reverse invasion fronts of their hosts. Biological Invasions **7**:817–832.

Hudson, P. J., A. Rizzoli, B. T. Grenfell, H. Heesterbeek, and A. P. Dobson. 2001. The ecology of wildlife disease. Oxford University Press, New York, New York, USA.

Jules, E. S., M. J. Kauffman, W. D. Ritts, and A. L. Carroll. 2002. Spread of an invasive pathogen over a variable landscape: A nonnative root rot on Port Orford cedar. Ecology **83**:3167–3181.

Kot, M., M. A. Lewis, and P. van den Driessche. 1996. Dispersal data and the spread of invading organisms. Ecology **77**:2027–2042.

Lafferty, K. D., and L. R. Gerber. 2002. Good medicine for conservation biology: the intersection of epidemiology and conservation theory. Conservation Biology **16**:593–604.

Lloyd-Smith, J. O., P. C. Cross, C. J. Briggs, M. Daugherty, W. M. Getz, J. Latto, M. S. Sánchez, A. B. Smith, and A. Swei. 2005. Should we expect population thresholds for wildlife disease? Trends in Ecology and Evolution **20**:511–519.

Loehle, C. 1995. Social barriers to pathogen transmission in wild animal populations. Ecology **76**:326–335.

Mackintosh, C. G., G. W. de Lisle, D. M. Collins, and J. F. T. Griffin. 2004. Mycobacterial diseases of deer. New Zealand Veterinary Journal **52**:163–174.

McCallum, H., and A. Dobson. 1995. Detecting disease and parasite threats to endangered species and ecosystems. Trends in Ecology and Evolution **10**:190–194.

McCarty, C. W., and M. W. Miller. 1998. A versatile model of disease transmission applied to forecasting bovine tuberculosis dynamics in white-tailed deer populations. Journal of Wildlife Diseases **34**:722–730.

Mollison, D. 1991. Dependence of epidemic and population velocities on basic parameters. Mathematical Biosciences **107**:255–287.

Morris, R. S., D. U. Pfeiffer, and R. Jackson. 1994. The epidemiology of *Mycobacterium bovis* infections. Veterinary Microbiology **40**:153–177.

Murray, J. D. 1993. Mathematical biology. Second edition. Springer-Verlag, New York, New York, USA.

Nugent, G. 1994. Home-range size and its development for fallow deer in the Blue Mountains, New Zealand. Acta Theriologica **39**:159–175.

O'Brien, D. J., S. M. Schmitt, J. S. Fierke, S. A. Hogle, S. R. Winterstein, T. M. Cooley, W. E. Moritz, K. L. Diegel, S. D. Fitzgerald, D. E. Berry, and J. B. Kaneene. 2002. Epidemiology of *Mycobacterium bovis* in free-ranging white-tailed deer, Michigan, USA, 1995–2000. Preventive Veterinary Medicine **54**:47–63.

Owen, M. R., and M. A. Lewis. 2001. How predation can slow, stop or reverse a prey invasion. Bulletin of Mathematical Biology **63**:655–684.

Perelberg, A. 2000. Ecological and behavioral aspects of the reintroduced Persian fallow deer population (*Dama dama mesopotamica*). Thesis. Tel Aviv University, Tel Aviv, Israel.

Perelberg, A., D. Saltz, S. Bar-David, A. Dolev, and Y. Yom-Tov. 2003. Seasonal and circadian changes in the home ranges of reintroduced Persian fallow deer. Journal of Wildlife Management **67**:485–492.

Prenter, J., C. MacNeil, J. T. A. Dick, and A. M. Dunn. 2004. Roles of parasites in animal invasions. Trends in Ecology and Evolution **19**:385–390.

Rodwell, T. C., N. P. Kriek, R. G. Bengis, I. J. Whyte, P. C. Viljoen, V. de Vos, and W. M. Boyce. 2001. Prevalence of bovine tuberculosis in African buffalo at Kruger National Park. Journal of Wildlife Diseases **37**:258–264.

Saltz, D. 1998. A long-term systematic approach to planning reintroductions: the Persian fallow deer and Arabian oryx in Israel. Animal Conservation **1**:245–252.

Scott, M. E. 1988. The impact of infection and disease on animal populations: implications for conservation biology. Conservation Biology **2**:40–56.

Shigesada, N., and K. Kawasaki. 1997. Biological invasions: theory and practice. Oxford University Press, New York, New York, USA.

Simberloff, D., and L. Gibbons. 2004. Now you see them, now you don't. Population crashes of established introduced species. Biological Invasions **6**:161–172.

Simpson, V. R. 2002. Wild animals as reservoirs of infectious diseases in the UK. Veterinary Journal **163**:128–146.

Sjöåen, T. 1997. Movements and establishment of reintroduced European otters *Lutra lutra*. Journal of Applied Ecology **34**: 1070–1080.

Tilman, D., and P. Kareiva. 1997. Spatial ecology: the role of space in population dynamics and interspecific interactions. Princeton University Press, Princeton, New Jersey, USA.

van den Bosch, F., R. Hengeveld, and J. A. J. Metz. 1992. Analysing the velocity of animal range expansion. Journal of Biogeography **19**:135–150.

Viggers, K. L., D. B. Lindenmayer, and D. M. Spratt. 1993. The importance of disease in reintroduction programs. Wildlife Research **20**:687–698.

Wahlström, H., L. Englund, T. Carpenter, U. Emanuelson, A. Engvall, and I. Vagsholm. 1998. A Reed-Frost model of the spread of tuberculosis within seven Swedish extensive farmed fallow deer herds. Preventive Veterinary Medicine **35**:181–193.

With, K. A. 2002. The landscape ecology of invasive spread. Conservation Biology **16**:1192–1203.

Woodroffe, R. 1999. Managing disease threats to wild mammals. Animal Conservation **2**:185–193.

APPENDIX A

A description of the simulation model (*Ecological Archives* E087-071-A1).

APPENDIX B

Model projection for disease extinction or growth over 20 years (*Ecological Archives* E087-071-A2).

APPENDIX C

Evaluation of the potential efficacy of four management strategies aiming to control disease spread (*Ecological Archives* E087-071-A3).