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Macroecological patterns of American Cutaneous Leishmaniasis transmission across the health areas of Panamá (1980–2012)

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ABSTRACT

American Cutaneous Leishmaniasis (ACL) is a neglected vector-borne zoonosis that persists despite increasing socio-economic development and urbanization in Panamá. Here, we investigate the association between environmental changes and spatio-temporal ACL transmission in the Republic of Panamá (1980–2012). We employ a macroecological approach, where patterns of variation in ACL incidence at the spatially coarse-grained scale of health areas are studied considering factors linked to the ecology of ACL transmission. We specifically study impacts of climatic variability, measured by the different phases of El Niño Southern Oscillation (ENSO), within diverse ecosystems and sand fly (Diptera: Psychodidae) vector species, as well as heterogeneous local climatic patterns, deforestation, population growth rates, and changes in social marginalization. We found that over the study period, patterns of ACL incidence: (i) were asynchronous with clusters changing from east to west of the Panamá Canal, (ii) trends increased in the west, and decreased or remained nearly constant in the east, independent of human population growth, (iii) generally increased in years following El Niño, and (iv) decreased as forest cover increased. We found no significant association between changes in socio-economic indicators and ACL transmission. Regarding vector abundance and presence, we found that studies had been biased to locations east of the Panamá canal, and that, in general, the abundance of dominant vector species decreased during the cold phase of ENSO. Finally, our results indicate that a macroecological approach is useful to understand heterogeneities related to environmental change impacts on ACL transmission.

1. Introduction

American Cutaneous Leishmaniasis (ACL) is a neglected vector-borne disease, closely associated with environmental change and poverty (Alvar et al., 2006; Wijeyaratne et al., 1994). Annually, around 66,000 new ACL cases are reported in the New

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World, and 2188 ACL cases occur annually in Panamá (Alvar et al., 2012). The reported cases are believed to account for only 1/3 to 1/2 of the real number of cases (Alvar et al., 2012; Christensen et al., 1999). In Panamá, ACL is mainly endemic and enzootic (Christensen et al., 1983, 1999; Miranda et al., 2009). The main ACL parasite is *Leishmania panamensis*. Nevertheless, a few cases due to other *Leishmania* spp. were reported a few decades ago (Christensen et al., 1983, 1999; Miranda et al., 2009; Grimaldi et al., 1989; Kreutzer et al., 1991). Vectors include several *Lutzomyia* spp., commonly known as sand flies (Diptera: Psychodidae), and as "chitras" in the Republic of Panamá. *Lutzomyia gomezi*, *Lu. panamensis*, and *Lu. trapidoi*, are the dominant vector species in Panamá (Christensen et al., 1983; Calzada et al., 2013; Chaves et al., 2013; Dutari and Loaiza, 2014). Proven enzootic mammal reservoirs include *Choloepus hoffmanni* (two-toed sloth), and several rodents, mainly rice (*Oryzomys* spp.) and spiny (*Proechimys* spp.) rats (Herrer and Telford, 1969; Herrer et al., 1971; Telford et al., 1972; Herrer and Christensen, 1976). Control for this disease in Panamá is currently focused on free clinical treatment for laboratory diagnosed cases, and relatively little attention has been given to strategies focused on vector control or that exploit the understanding of ACL transmission eco-epidemiology (Chaves et al., 2013; Saldaña et al., 2013). However, recently, the number of ACL cases has been increasing in the Republic of Panamá (Saldaña et al., 2013), and renewed efforts to understand ACL eco-epidemiology and to improve ACL vector control and ACL diagnostics have been carried out in Panamá (Calzada et al., 2013; Chaves et al., 2013; Saldaña et al., 2013; Miranda et al., 2012). Moreover, the increasing trend in ACL incidence contradicts previous proposals that socio-economic development and urbanization would eliminate the disease (Herrer and Christensen, 1976; Christensen and de Vasquez, 1982).

It is unclear what has been driving ACL incidence changes in Panamá. Competing hypotheses for the recent increase in ACL incidence include: (1) shifts of reservoir hosts from wildlife (Herrer and Telford, 1969; Herrer et al., 1971, 1973; Telford et al., 1972) to domestic mammals (Calzada et al., 2015a; Travi et al., 2006; Chaves et al., 2007); (2) changes in vector species composition (Calzada et al., 2013; Valderrama et al., 2008, 2011); (3) human population increase in endemic areas (Alvar et al., 2012; Chaves et al., 2008a), and (4) transmission exacerbation due to climate change impacts on vectors and reservoirs against a background of socio-economic inequity (Chaves et al., 2008a). Our research has shown that shifts on major ACL mammal reservoir species seem unlikely (Calzada et al., 2015a; González et al., 2015), and that changes in sand fly species composition has not affected dominant vector species (Christensen et al., 1983; Dutari and Loaiza, 2014; Calzada et al., 2013). However, it is still unclear to what degree ACL transmission trends could reflect demographic changes, such as population growth in endemic areas (Alvar et al., 2012) or different degrees in vulnerability to ACL that could be associated with: socio-economic conditions (Chaves et al., 2008a, 2013; Levins and Lopez, 1999), deforestation (Wijeyaratne et al., 1994), or whether the emergent patterns of ACL transmission echo changes in climate variability (Chaves et al., 2008a; Patz and Olson, 2006).

The large scale of environmental changes and other heterogeneities associated with hypotheses (3) and (4) require coarse-grained macroecological analyses, in the sense that new knowledge can be derived by looking at how the context influences the distribution and abundance of a disease across populations, not individuals (Susser, 1994a; Keyes and Galea, 2014). More specifically, integral variables, i.e., those affecting all or virtually all members of a population (Susser, 1994a), as in the case of climatic phenomena, such as El Niño Southern Oscillation (ENSO) in Panamá, and contextual variables, the mean, median or proportion of an attribute (Susser, 1994a), for example forest cover or poverty within a geopolitical unit, are best studied at the population level. Therefore, this type of study is "macroecological" (Brown, 1995) since the scaling-up of the "ecological" analysis to spatially and temporally relatively coarsely grained scales (Levin, 1992), with all its sacrifice of detail (Brown, 1995), is still helpful to understand patterns of variation (Levins, 1995) in the distribution and incidence of a disease, in the same way the "macroecological" approach has been used to study populations in ecology (Brown, 1995).

Concerning the impacts of climate change on ACL in Central America, in both Costa Rica (Chaves et al., 2008a; Chaves and Pascual, 2006, 2007; Chaves, 2009) and the Republic of Panamá (Chaves et al., 2014a) interannual cycles in ACL incidence are associated with ENSO. Furthermore, it has also been observed that strong fluctuations in sand fly abundance are associated with ENSO in the Republic of Panamá (Chaves et al., 2014a). Nevertheless, it is unclear how homogeneous/heterogeneous the impacts of ENSO across the Republic of Panamá are, where local variations exist in seasonal weather, the east of the country being slightly more wet than the west (Autoridad Nacional del Ambiente, 2010). Although rainfall is concentrated during the rainy season, which spans from April to December over most of the country, its duration can be slightly shorter towards the west (Autoridad Nacional del Ambiente, 2010). Although temperatures tend to be near constant throughout the country, temperature is slightly lower on the Pacific basin than on the Caribbean basin of the Panamá isthmus (Autoridad Nacional del Ambiente, 2010). Likewise, following global patterns, temperature declines with altitude (Chaves and Koenraadt, 2010). In Panamá, local impacts of ENSO are characterized by a reduction of rainfall over the Pacific coast and an increase of rainfall on the Caribbean coast, during the hot phase (a.k.a., El Niño) of the oscillation, with droughts accentuated during the cold phase (a.k.a., La Niña) of ENSO (Olmedo, 2006). On top of weather heterogeneities, the Republic of Panamá has a wide diversity of natural ecosystems, ranging from dry forests to tropical rainforests, and all the ecosystems have been subjected to different changes in land use over the last 50 years, with heterogeneous deforestation rates rendering a heterogeneous degree of forest cover across the country (Autoridad Nacional del Ambiente, 2010).

The heterogeneity of environmental patterns in Panamá raise questions on whether: (i) ENSO impacts on ACL transmission across the Republic of Panamá are homogenous, and whether patterns are synchronous, with ACL incidence fluctuating in concert across Panamá's Health areas (ii) disease clusters and differential impacts of ENSO are more likely to occur in regions where poverty, or its proxies, are more prominent, (iii) trends in ACL transmission simply reflect population increase and (iv) differential impacts of ENSO, associated or independent of the dominant ecosystem type or contextual forest cover could have led to the