Trends in Parasitology

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Zoonotic and Vector-Borne Diseases in Urban Slums: Opportunities for Intervention

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Urban slums provide conditions that increase the risk of exposure to vector-borne and zoonotic pathogens. Large interventions, such as social and sanitary changes, are a priority but their implementation is challenging. Integration between the multidisciplinary understanding of pathogens' dynamics and community participatory approaches is a key prevention strategy.

As the UN-Habitat [1] report notes: 'although urbanization has the potential to make cities more prosperous and countries more developed, many cities all over the world are grossly unprepared for the multidimensional challenges associated with urbanization'. The term 'urban planning' is an oxymoron when applied to the sprawl of major tropical cities in developing countries where the unplanned and uncontrollable growth of slums is often juxtaposed among gated communities, presenting a constantly shifting target. Irrespective of physical development plans, planning for urban health, taking into account socioeconomic disparities, remains in its infancy. UN-Habitat [1] defines a slum household as one where the inhabitants are affected by the lack of at least one of the following: access to an improved source of water, access to improved sanitation facilities, sufficient living area, housing durability, and security of tenure. These factors contribute to and compound socioeconomic inequities, including poor access to formal jobs and critical social services (e.g., education and healthcare), which result in decreasing quality of life, poor health, and a shorter life expectancy. Paradoxically, slum formation was initially driven by rural migrants seeking job opportunities and education. The number of slum residents increased by 28% between 1990 and 2014, from 689 million to 881 million, and it is likely that another 600 million will lack decent housing between 2010 and 2030 [1].

By the nature of poverty, with inadequate housing and water–sanitation infrastructure, slum dwellers are at increased risk for exposure to zoonotic pathogens resident in mammalian reservoirs or transmitted directly among humans by arthropod vectors. Slum expansion frequently promotes environmental degradation and decreases biological diversity, leading to an environment favorable for enhancing populations of notorious mammalian reservoir species (e.g., *Rattus norvegicus*) and the 'container breeding' mosquito *Aedes aegypti*. As exemplified by urban centers throughout Brazil, Norway rat-borne pathogens, notably *Leptospira*, and *Ae. aegypti*-vectored viruses, such as dengue virus and epidemic Zika virus (ZIKV), disproportionately afflict marginalized slum populations [2,3].

While most infectious diseases have decreased in morbidity and mortality through vaccine initiatives and interventions to ameliorate diarrheal disease, vector-borne and zoonotic diseases (VBZDs) in urban slums (e.g., ZIKV disease, dengue and leptospirosis) have experienced no reduction in disease burden. Control failures are attributable to the complex patterns of intraspecific and interspecific pathogen transmission comprising environmental, socioeconomic determinants and the inherent difficulties in controlling for pathogens maintained in zoonotic reservoirs or in urban-adapted mosquitoes [4,5]. A key challenge in preventing and controlling VBZDs is the failure to develop multidisciplinary understanding of the link between reservoir dynamics and human health; these issues fall within the 'One Health' paradigm, requiring collaboration among veterinary and human health professionals, environmental scientists, and social scientists. Herein we focus on two VBZDs, first, leptospirosis, a long-established zoonosis, and second, ZIKV disease, an emerging vector-borne disease.

Leptospirosis is a disease that disproportionately burdens the most impoverished segments of the world's population. The etiologic agent, a spirochete, is excreted in the urine of reservoir hosts, primarily Norway rats in urban settings. Worldwide, leptospirosis is estimated to cause more than 1 million cases and 60 000 deaths annually, with a large proportion in tropical urban slums [2]. Beginning in 1996, we identified seasonal periods of heavy rainfall with epidemics affecting slum communities and linked transmission to peridomestic Norway rat infestations around individual households [6]. Norway rats in these settings are abundant and, in contrast to temperate cities, reproduce throughout the year. Rat abundance is heterogeneous, varying between closely adjacent sites, with increased numbers associated with human density, access to open sewers, and sources of food – factors that reflect the overcrowding, lack of improved sanitation, or even the housing durability. In summary, the conditions that favor rat populations are the same as those that define urban slums [1]. The prevalence of *Leptospira* in the kidneys and urine of rats is extremely high (>80%), and a population of ~100 rats sheds >1 billion leptospires per day into the environment [7]. Leptospires that are shed into the environment are the primary source of human infection through penetration of skin abrasions.

While slums are able to support large populations of rats, transmission to humans is additionally influenced by the frequency of contact with contaminated water and/or soil. In Salvador slums, for example, lack of improved sanitation, combined with the steep topology (with the most impoverished people living at the bottom of valleys), create flooded areas and thick mud contaminated with pathogenic bacteria dislodged from soil. Household elevation (a proxy of distance to open sewers) (OR 0.92, 95% CI 0.82–1.04 for each 10 m increase in elevation) and contact with contaminated mud (OR 1.57, 95% CI 1.13–2.17) were found to increase the risk of human infection [8]. Those distinct differences in the microenvironment lead to a substantial spatial variation in the risk of *Leptospira* infection. Additionally, residents' individual characteristics – specifically, young age, male gender, and low education status – are associated with risky behaviors leading to higher exposure to contaminated environments [8].

In the second example, ZIKV is an emerging mosquito-borne flavivirus discovered in Africa in 1947. For most of its history, ZIKV has raised little concern, based on the paucity of reported cases and disease limited to rash and fever. However, since its introduction to South American countries, ZIKV has been associated with large epidemics of clinical disease, including exanthematic disease, Guillain–Barré syndrome affecting adults, and congenital ZIKV syndrome in newborns, which can result in microcephaly and other severe manifestations [5]. In Brazil, a total of 2106 confirmed cases with microcephaly were reported by October 2016. Data aggregated at the state level in Brazil have shown that low socioeconomic status may also increase transmission: incidence of ZIKV microcephaly has shown a negative association ($r = -0.64$) with gross domestic product (GDP) per capita [9]. Unsurprisingly, in Rio de Janeiro, Brazil, ZIKV exanthematic disease has clustered in the same slums affected by dengue epidemics [3], suggesting similar socioenvironmental determinants of transmission. Lack of infrastructure, exemplified by absence of, or intermittent, water supply, is responsible for the conditions that are suitable for the breeding of *Ae. aegypti*. Concomitant high mosquito density and human overcrowding is likely to facilitate virus transmission by increasing human–mosquito–human contact. Governmental efforts to control dengue – by focusing on *Ae. aegypti* larval and adult control – have mostly been unsuccessful [5], and there is no reason to expect better results with ZIKV disease. As with rat-borne leptospirosis, the defining features of slums [1] compound the inherent difficulties of controlling VBZDs.

VBZDs in the slums are associated with macro-socioenvironmental determinants of health, but large-scale interventions to generate changes in those determinants are universal challenges. Examples of successes with controlling non-VBZDs come through nationwide programs initiated in Brazil and Mexico. Conditional cash transfer programs can decrease child mortality from general and infectious disease causes (e.g., diarrhea) by acting on social determinants of health. Families enrolled in these programs must comply with specific education and health-related conditions (children need to attend school and receive routine health care, including vaccination) [10]. Additionally, large-scale efforts to improve sanitary conditions through covering open sewers flowing within slums (from 26% of households to 80%) are estimated to have reduced the incidence of severe diarrheal disease by 21% in a 5-year period [11]. Coincidently, we identified a 45% decline in leptospirosis incidence in Salvador over the same period (information obtained from the SINAN, Sistema de Informação de Agravos de Notificação, database system – http://www2.datasus.gov.br/DATASUS/index.php?area=0203&id=29878153), suggesting that improved sanitation may have an impact in preventing leptospirosis. Improved rainwater drainage, sewage, and sanitary measures may play a role in decreasing VBZD transmission by blocking access to resources needed by rats and mosquitoes, but systematic assessments are lacking and badly needed. The broad aim of combatting poverty and social inequity requires long-term agendas, which are often not practical given budgetary constraints. The daily lack of sanitation and poor infrastructure conditions in slums, which expose residents to VBZDs, require creative and local approaches that fit the community needs in overcoming these barriers. Improved community-based strategies to control VBZDs in urban slums have focused mainly on dengue and malaria. Community-based strategies to prevent dengue include behavioral and educational campaigns coupled with biological/chemical control techniques [5], but little evidence exists to support the efficacy of those control programs in decreasing entomological or human disease indicators. In contrast, community-based programs for malaria prevention have shown improvements in reducing transmission in urban settings, mainly through modification of irrigation structures [12]. Housing improvement to restrict mosquito ingression (e.g., closing gaps in the eaves) can lower the risk of malaria transmission in urban settings [13], and as a basic environmental intervention could impact both vector- and rodent-borne infections in other settings. Regarding rodent-borne diseases, very few studies have been published showing the effectiveness of rodent control in urban slums, and as for dengue, most of the results show only short-term effectiveness in decreasing rodent abundance, or none at all, and no evidence of effects on disease transmission.

Infrastructural changes, such as sewer and sanitary modifications, and improved housing to decrease the vector's foci and rodent ingression, are the first candidates for implementation. However, those methods require not only materials, monetary investment, and infrastructural organization, but also sustained commitment by local, community, and governmental parties. Local interventions, and in particular a participatory action research (PAR) approach, may provide more effective long-term solutions. Under PAR, individuals in the communities are key to the process of determining which issues are critical to their welfare and actively collaborate with research professionals in designing programs. At its best, PAR community members are empowered by helping to shape a future which reduces inequities in access to resources, and they share the responsibility of perpetuating involvement through subsequent generations. Two examples of the success of PAR with VBZDs provide an optimistic note to what at first glance seem intractable problems. In Guantanamo, Cuba [14], an interdisciplinary research team and community members identified local needs and priorities for environmental control of dengue, subsequently resulting in a 50% reduction in *Aedes* infestation. PAR has also been successful in controlling Chagas, in Guatemala, by controlling reservoir rodents through participatory education and training in mechanical rodent control [15].

The complexity of factors that characterize slums make this urban setting a stage for the transmission and emergence of VBZDs. Large-scale interventions able to change social and environmental inequalities are critical for decreasing the impact of VBZDs, but the expansion rate and magnitude of urban slums is constraining attempts to achieve these goals. This emphasizes the urgency of developing effective and sustainable community-based interventions to interrupt disease transmission and reduce disease burdens in the long term. Moreover, to be successful, this strategy should integrate behavioral, environmental, and biologic interventions, together with effective participatory approaches.

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