Integrated disease mapping in a polyparasitic world

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Malaria and the neglected tropical diseases

In the past, and still today, people living in the developing world have been, and continue to be, repeatedly exposed to a number of endemic parasitic diseases which impose an intolerable economic, health and social burden on their societies (Stoll, 1947; Sachs and Malaney, 2002). Among the parasitic diseases, malaria due to Plasmodium falciparum inflicts the largest burden (Snow et al., 2005). Concurrently, hundreds of millions of people are plagued by a number of so-called neglected tropical diseases (NTDs). The most significant of these are Chagas disease in South America, human African trypanosomiasis, leishmaniasis, lymphatic filariasis, onchocerciasis, schistosomiasis, soil-transmitted helminthiasis and trachoma. The scale of the problem is illustrated in Table 1, which summarises current population statistics, including at-risk populations, estimated numbers of people infected, annual morbidity and mortality rates and burden estimates due to malaria and the above-mentioned NTDs.

In recent years, there has been an upsurge in public and private spending in global health, with particular efforts aimed at tackling HIV/AIDS, tuberculosis and malaria (Lu et al., 2006). With enhanced funding coming on stream also for the NTDs, new partnerships and global alliances have been formed to tackle a number of NTDs, with preventive chemotherapy playing a key role (Brady et al., 2006; Hotez et al., 2006; WHO, 2006). This funding has coincided with calls to improve the coordination and integration of national control programmes, placing emphasis on simultaneous morbidity control due to NTDs (e.g. schistosomiasis and soil-transmitted helminthiasis) or to eliminate NTDs as a publichealth problem (e.g. lymphatic filariasis) (Brady et al., 2006; Lammie et al., 2006). To help allocate public-health resources, an essential first step is to delineate and understand the spatial distribution of different parasitic diseases (Brooker et al., 2006; Hay and Snow, 2006; Utzinger and de Savigny, 2006).

Mapping and prediction of co-endemic areas

The need

Parasite transmission intensity exhibits significant spatial and temporal heterogeneity and, because of their neglected nature, there exists limited information about the exact geographical distribution of most of the NTDs, as well as malaria (Polack et al., 2005; Hay and Snow, 2006). It follows that the spatial congruence of different NTDs, as well as of

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Table 1. Current global estimates of populations at risk, number of people infected and suffering from morbidity, and annual mortality rates and burden estimates of malaria and selected NTDs (DALY, disability-adjusted life year; NA, not applicable; ND, not determined). The DALY is a summary measure of disease burden that combines the impact of illness, disability and mortality on population health and was last estimated by the World Health Organization in 2002 (http://www.who.int/health-info/bod/en/index.html).

Disease	Causative agent(s)	Population at risk (x 10 ⁶)	People infected (x 10 ⁶)	Morbidity (x 10 ⁶)	Mortality (x 10 ³)	Burden (x 10 ⁶ DALYs)	Reference
Malaria	Plasmodium falciparum, P. malariae, P. ovale, P. vivax	2211	NA	515	1272	46.49	WHO, 2004; Snow et al., 2005
Soil-transmitted helminthiasis							
Ascariasis	Ascaris lumbricoides	4211	807-1221	350	3-60	1.82-10.5	Bethony et al., 2006; Lammie et al., 2006
Hookworm disease	Ancylostoma duodenale, Necator americanus	3195	576-740	150	3-65	0.06-22.1	Bethony et al., 2006; Lammie et al., 2006
Trichuriasis	Trichuris trichiura	3212	604-795	220	3-10	1.01-6.4	Bethony et al., 2006; Lammie et al., 2006
Strongyloidiasis	Strongyloides stercoralis	ND	30-100	ND	ND	ND	Bethony et al., 2006
Lymphatic filariasis	Wuchereria bancrofti, Brugia malayi, B. timori	>1000	120	43	0	5.78	Lammie et al., 2006
Schistosomiasis	Schistosoma haematobium, S. intercalatum, S. japonicum, S. mansoni, S. mekongi	779	207	120	15-280	1.7-4.5	Lammie et al., 2006
Trachoma	Chlamydia trachomatis	ND	150	ND	0	2.33	WHO, 2004
Onchocerciasis	Onchocerca volvulus	120	18	ND	0	0.48	Watkins, 2003; WHO, 2004
Leishmaniasis	Leishmania donovani, L. chagasi, L. infantum	350	12	ND	51	2.09	Watkins, 2003; WHO, 2004
Human African trypasosomiasis	Trypanosoma brucei gambiense, T. b. rhodesiense	>60	0.5	ND	50	1.53	Watkins, 2003; WHO, 2004
Chagas disease	Trypanosoma cruzi	120	11-18	ND	13	0.67	Watkins, 2003; WHO, 2004

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NTDs and *P. falciparum* malaria, remains poorly defined. On the other hand, significant progress has been made with a number of geospatial tools, such as geographical information systems (GIS), remotely-sensed environmental data, and geostatistics that allow to better describe, understand and predict the geographical distribution of single NTDs (Malone, 2005; Yang et al., 2005; Brooker, 2007). Ultimately, these geospatial tools offer the potential to improve the spatio-temporal targeting of control measures and to enhance the cost-effectiveness of integrated disease control programmes.

The proposal

In the context of integrated disease control, we propose that the spatial co-distribution of different parasite species over large geographical areas, such as at continental scales, can be based initially on climate-based disease risk maps (Brooker et al., 2006). Such maps, however, belie the geographical variation of co-distribution and co-infection evident at community and district levels, which is difficult to capture with existing risk models. To date, only one study has attempted to analyse the spatial occurrence of co-infection at a small spatial scale (an area of 40 x 60 km) within a single district of a West African country (Raso et al., 2006). This study showed that it was possible to predict spatial patterns of *Schistosoma mansoni*-hookworm co-infection.

tions. Future similar work for different parasite species in varying transmission settings, coupled with an improved understanding of spatial risk factors of different parasite species will allow the projection of co-endemicity on the basis of remotelysensed satellite data, as well as behavioural, demographic, epidemiological and socio-economic risk factors. Such research will aid the development of risk maps which can identify large-scale patterns of potential overlap, and thus guide regional and national level integrated disease control efforts.

At finer scales, on the other hand, there remains a need to undertake rapid and inexpensive assessments of infection levels to guide local control. Table 2 summarises different approaches that have been developed and successfully validated for the rapid assessment of different NTDs. For example, a simple morbidity questionnaire administered through the existing education system allows the rapid delineation of high-risk areas of schistosomiasis haematobia, based on the specific symptomatology of Schistosoma haematobium, which is the presence of blood in urine (Lengeler et al., 2002). With regard to lymphatic filariasis, onchocerciasis and visceral leishmaniasis, accurate, non-invasive, rapid antigen detection assays applicable under field conditions have become available (Weil et al., 1997; Ayong et al., 2005; Chappuis et al., 2006). In the case of lymphatic filariasis, mapping of disease distributions has been based on the use immunochro-

Disease	Causative agent(s)	Rapid assessment approach	Reference
Schistosomiasis	Schistosoma haematobium	Morbidity questionnaires: reported blood in urine	Lengeler et al., 2002
	Schistosoma mansoni	osoma mansoni Morbidity questionnaires: reported blood in stool	
		Close proximity to lakes (< 5 km)	Lengeler et al., 2002
		Lot quality assurance sampling	Brooker et al., 2005
	Schistosoma japonicum	Morbidity questionnaires: reported blood in stool	Zhou et al., 1998
Lymphatic filariasis	Wuchereria bancrofti	Antigen detection assay: ICT	Weil et al., 1997
		Lot quality assurance sampling	Vanamail et al., 2006
Leishmaniasis	Leishmania donovani, L. chagasi, L. infantum	Antigen detection assay: K39 strip test	Chappuis et al., 2006
Onchocerciasis	Onchocerca volvulus	Antigen detection assay: Oncho-dipstick test	Ayong et al., 2005

Table 2. Tools currently available for rapid and inexpensive assessment of high-risk communities, and hence for mapping purposes, of a number of NTDs.

matographic card tests (ICT) for the detection of circulating antigen from adult *Wuchereria bancrofti* filarial antigenaemia in order to target mass drug administration (Gyapong et al., 2002).

Recent operational research has also highlighted the potential of lot quality assurance sampling of a small number of individuals attending primary schools for identifying high-risk communities for schistosomiasis mansoni (Brooker et al., 2005) and for monitoring lymphatic filariasis control programmes (Vanamail et al., 2006). Further investigation and comparison of the cost-effectiveness of different rapid mapping approaches, used singly or in combination, is clearly warranted. We conjecture that it should be possible to integrate the rapid mapping of different NTDs simultaneously with tools that are already available, and that this is an area which merits investigation.

Challenges and opportunities

A major challenge for such geospatial research will be to integrate the disease-specific ecologies and epidemiologies of different parasite species and vector/intermediate host species, as well as contextual determinants (e.g. behaviour, density and migration patterns of humans and socio-economic status) into a single analytical framework. For example, recent studies have highlighted intrinsic differences in the spatial heterogeneity of specific diseases depending on the eco-epidemiological and socio-cultural setting (Gyapong et al., 2002; Brooker et al., 2004). Hence, understanding the complexity of risk factors of co-distribution and co-infection require detailed field studies, including validation of generated risk maps of co-infections. The studies will also necessitate the development of new geostatistical methods, building on the successful application of Bayesian geostatistical approaches in modelling spatial distributions of single parasite species (Gemperli et al., 2004; Raso et al., 2005; Clements et al., 2006).

Finally, the development of an integrated approach to map and predict a number of different NTDs simultaneously would require careful consideration of the different spatial heterogeneities of different species and over what spatial scale variation occurs, as well as simulation studies to determine the optimal sample size to capture species-specific epidemiological patterns.

Concluding remarks

As public-health resources are increasingly available to address global health issues as part of unprecedented efforts to meet international development goals, large-scale control efforts get underway, most recently also to tackle NTDs. The initiation of such control does not, however, signal the end of geospatial research rather underscores its vital importance. Numerous geospatial issues require attention, including geostatistical techniques that should go hand-in-hand with field studies and operational research, thus requiring collaboration among geospatial scientists and public-health specialists. Such work will determine whether research can have a real public-health impact rather than remain only an academic exercise.

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