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FAMILIAL AGGREGATION AND HERITABILITY OF *WUCHERERIA BANCROFTI* LYMPHATIC FILARIASIS

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Lymphatic filariasis (LF) is responsible for severe disabilities across the world, especially because of lymphedema. Although immune factors were identified to explain the development of lymphedema in infected individuals, few studies have investigated the genetic susceptibility to infection. To assess familial aggregation and heritability of ***Wuchereria bancrofti*** infection, we conducted a study in a village of the Republic of Congo. Pedigree was built for 829 individuals (broken down in 267 households and 36 families) from which 143 were positive at the immunochromatographic card test (prevalence: 17.3%) and 44 (5.3%) had ***W. bancrofti*** microfilariae (mf). Analyses were adjusted on individual risk factors for LF (age, sex, outdoor activities, usage of bednet) and for environmental factors (eg: distance between house and nearest river), and accounted for possible household effect. Patterns of familial aggregation, assessed using S.A.G.E. software, showed that the presence of antigenemia was very slightly but significantly correlated within families ($0.06 < r < 0.10$; with $0.001 <$ P-value < 0.013). Regarding microfilaremia, correlation values were much higher: $r = 0.45$ between fathers and sons (P-value = 0.013), $r = 0.78$ between mothers and sons (P-value = 0.034), and $r = 0.94$ between fathers and daughters (P-value < 0.001). Heritability was estimated using SOLAR software. Genetic factors explained 13% (P-value = 0.226), 61% (P-value = 0.166) and 51% (P-value = 0.048) of variation in the presence of antigenemia, presence of mf, and in mf density, respectively. Household effect was never found significant. Our results show that the acquisition of ***W. bancrofti*** infection (as assessed by antigenemia) barely depends on genetic factors and is thus mainly due to exposure factors. However, both the presence of mf and variation in ***W. bancrofti*** mf density seem significantly influenced by genetic factors. Additional genetic studies are needed to confirm this finding.

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HUMAN ONCHOCERCIASIS: MODELLING THE POTENTIAL LONG-TERM CONSEQUENCES OF A VACCINATION PROGRAM

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Currently, the predominant onchocerciasis control strategy in Africa is annual mass drug administration (MDA) with ivermectin. However, there is a consensus among the global health community, supported by mathematical modelling, that onchocerciasis in Africa will not be eliminated within proposed time frameworks in all endemic ***foci*** with only annual MDA, and that novel and alternative strategies are urgently needed. Furthermore, use of MDA with ivermectin is already compromised in large areas of central Africa co-endemic with loiasis and there are areas where suboptimal or atypical responses to ivermectin have been documented. An onchocerciasis vaccine would be highly advantageous in these areas. We used a previously developed onchocerciasis transmission model (EPIONCHO) to investigate the impact of vaccination in areas where loiasis and onchocerciasis are co-endemic and ivermectin is contraindicated. We also explore the potential influence of a vaccination programme on infection resurgence in areas where local elimination has been successfully achieved. Based on the age range included in the Expanded Programme on Immunization (EPI), the vaccine was assumed to target 1 to 5 year olds. Our modelling results indicate that the deployment of an onchocerciasis vaccine would have a beneficial impact in onchocerciasis-loiasis co-endemic areas, markedly reducing microfilarial load in the young (under 20 yr) age groups. An onchocerciasis vaccine would reduce the onchocerciasis disease burden in populations where ivermectin cannot be administered safely. Moreover, a vaccine could substantially decrease the chance of re-emergence of ***Onchocerca volvulus*** infection in areas where it is deemed that MDA with ivermectin can be stopped. Therefore, a vaccine would protect the substantial investments made by present and past onchocerciasis control programmes, decreasing the chance of disease recrudescence and offering an important additional tool to mitigate the potentially devastating impact of emerging ivermectin resistance.

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IMMUNO-EPIDEMIOLOGY OF SOIL-TRANSMITTED HELMINTH INFECTIONS AFTER REPEATED SCHOOL-BASED DEWORMING: A COMMUNITY-WIDE CROSS SECTIONAL STUDY IN WESTERN KENYA

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The development of human immunity to soil-transmitted helminths remains poorly understood despite their widespread endemicity in tropical and subtropical countries. Infected individuals in endemic areas do not appear to develop fully protective immune responses, and the factors driving possible partial immunity acquired are unclear. With the increasing number of endemic countries introducing school-based deworming programs, there is a need to understand the effect of anthelminthic treatment on immune responses to helminths, not only in school-age children but also in younger and older members of the treated community. This study investigates both the development of humoral immunity against ***Ascaris lumbricoides*** and hookworm in an endemic community, and the effect of school-based and community-based anthelminthic treatment on antibody responses. The study took place in 2014 in four villages of Bungoma County, Western Kenya, where annual school-based deworming has been taking place since 2012. Stool and finger-prick blood samples were collected from over 1300 individuals aged 2 to 88 years, before and three months following community-wide treatment with 400mg albendazole. Parasite egg counts were obtained using Kato-Katz thick smears and antibody seroprevalence was measured by enzyme-linked immunosorbent assay (ELISA). Prevalence of ***A. lumbricoides*** and hookworm infections was 7.3% and 6.2%, respectively, at study baseline, and 2.6% and 2.0% at follow-up. Individual antibody profiles against ***A. suum*** haemoglobin (AsHb) and ***Necator americanus*** larval (Na-ASP2) and adult (Na-SSA-2) antigens were obtained and analysed by age-group, village and population level. Correlations between antibody seroprevalence and intensity of soil-transmitted helminth infection were investigated at both sampling time-points, taking into consideration a series of confounding factors including malaria co-infection and socio-economic and hygiene and sanitation ranks. Changes in antibody seroprevalence levels post community treatment with albendazole were also investigated, with particular emphasis on differences between age-groups.