Combining a Novel Immunoassay to Quantify Antibodies to Salivary Antigens with Antibody Acquisition Models to Estimate Exposure to *Simulium damnosum* s.l. Bites

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Background:
Human onchocerciasis is caused by the filarial nematode *Onchocerca volvulus* and spread by the bites of *Simulium* blackfly vectors. Exposure to blackfly bites is a key driver of transmission and success of interventions. We combine a novel enzyme-linked immunosorbent assay (ELISA) that measures IgG antibody levels against salivary antigens of *S. damnosum* s.l. collected from four onchocerciasis-endemic villages of the Bono East region of Ghana with antibody acquisition models designed to capture the change in antibody levels with age and sex, as a tool to identify patterns of exposure to vector bites.

Methods:
Three alternative antibody acquisition models, described by ordinary differential equations, were constructed to model the dynamics of anti-blackfly salivary IgG antibody titre by age and sex. The models assume that exposure to blackfly bites (and concurrently to salivary antigens) increases antibody levels, with antibody decaying at a constant rate through time. The models are: (**1**) *exposure only*, age- and sex-specific exposure to blackfly bites, such that exposure to bites can increase or decrease with age independently for either sex; (**2**) *desensitisations in antibody acquisition*, age- and sex-specific exposure to blackfly bites with cumulative past exposure to bites reducing antibody acquisition for a given exposure; (**3**) *desensitisation in antibody decay*: age- and sex-specific exposure to blackfly bites with cumulative past exposure to bites accelerating antibody decay. All three models were fitted to ELISA-derived standardised optical density titres of anti-blackfly saliva IgG antibodies from 958 individuals. The exposure functions derived from each model were incorporated into an individual-based, stochastic, onchocerciasis transmission model (EPIONCHO-IBM) to evaluate how the different exposure functions to blackfly bites alter the predicted age- and sex-specific profiles of microfilarial load by comparing to data from the same region in Ghana. We also assessed the impact on onchocerciasis community-directed treatment with ivermectin (CDTI) programmes.

Results:
All three antibody acquisition models captured the observed IgG dynamics but resulted in different predicted patterns of exposure to blackfly bites. Models (2) and (3) fitted the IgG data better, producing patterns of exposure that were consistent with previous estimates, and resulted in predicted age and sex profiles of microfilarial load resembling pre-intervention infection patterns from the same region in Ghana when incorporated into EPIONCHO-IBM. The different exposure patterns thus generated produced different predicted age and sex infection profiles after multiple years of CDTI, notably in children.

Discussion/Conclusion:
Human antibody responses to blackfly salivary antigens have the potential to represent an invaluable tool to measure exposure to blackfly bites at both individual and population levels, with implications for onchocerciasis morbidity, control, elimination and surveillance. The antibody acquisition models offer a way to link antibody data to exposure functions, that can be used within transmission models. The precise inference of exposure from such assays depends on immunological assumptions that warrant further study.

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