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SHORT REPORT: PROXIMITY TO MOSQUITO BREEDING SITES AS A RISK FACTOR FOR CLINICAL MALARIA EPISODES IN AN URBAN COHORT OF UGANDAN CHILDREN

SARAH G. STAEDKE, E. WILLIS NOTTINGHAM, JONATHAN COX, MOSES R. KAMYA, PHILIP J. ROSENTHAL, AND GRANT DORSEY

Department of Medicine, San Francisco General Hospital, University of California, San Francisco, California; Makerere University Medical School, Kampala, Uganda; Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, United Kingdom

Abstract. The impact of geography on incidence of clinical episodes of malaria was investigated in a cohort of children enrolled in a longitudinal clinical trial of antimalarial therapy in Kampala, Uganda. Participant households and the boundaries of local swamps and streams were mapped and incidence of clinical malaria episodes was measured prospectively using passive surveillance during one year of follow-up. Of 316 cohort participants, 305 from 219 households were followed for at least six weeks and were included in the analysis. Incidence of clinical malaria was highly variable, with no episodes occurring in 131 participants, and 367 new episodes of malaria diagnosed in the remaining 174 children. A gradient in incidence of clinical episodes of malaria was observed with distance of residence from a swamp (0.41 episodes per person year for residence >100 meters from a swamp increasing to 2.22 episodes per person year for residence within a swamp), or a stream (0.61 episodes per person year for residence >500 meters from a stream versus 1.76 episodes per person year for residence <500 meters from a stream). Multivariate analysis showed that distances of residence from a swamp or from a stream were independent predictors of malaria incidence, controlling for age, use of preventative measures, and primary source of water. Distance from a swamp was the strongest predictor, with an incidence rate ratio of 4.3 (95% confidence interval = 2.6-6.9, P < 0.001) between residence within a swamp and >100 meters from a swamp. In this urban setting, incidence of clinical episodes of malaria was strongly associated with proximity of residence to potential mosquito breeding sites.
ing was taken. Similar readings were taken for the boundaries of the division and local swamps and streams. A swamp was defined as a low-lying area with frequent standing water, particularly in times of steady rainfall. Distances of households to swamps and streams within Kawempe were calculated using ARC/INFO GIS software (Version 7; Environmental Systems Research Institute, Redlands, CA).

Malaria incidence density was defined as the number of new episodes of malaria per time at risk. Independent predictors of malaria incidence density were identified using a multivariate negative binomial regression model, controlling for clustering of clinical episodes of malaria for participants living in the same household and other risk factors previously identified including age, primary source of water, and use of malaria preventative measures. Statistical analysis was performed using STATA statistical software (Stata Corporation, College Station, TX).

Of the 316 subjects enrolled in the primary study, 305 from 219 households completed at least six weeks of follow-up, and were included in the analysis. The follow-up period covered approximately the same calendar year for all subjects. The cumulative period of observation in the primary cohort covered 93% of potential follow-up time, and 282 subjects (89%) completed the full one-year of follow-up. Parasite prevalence served with residence ≥500 meters compared with residence <500 meters from a stream (Table 1). Multivariate analysis, controlling for other previously identified risk factors, showed that distance of residence from a swamp and from a stream were independent predictors of incidence of clinical episodes of malaria; distance from a swamp was the stronger predictor (Table 2).

In this study, we prospectively measured the association between proximity of residence to vector breeding sites and episodes of clinical malaria over an extended risk period, controlling for other potential risk factors. In this urban cohort, residence near potential mosquito breeding sites was associated with an increased risk of clinical malaria episodes. Distance of a household from a swamp appeared to be a more important factor than distance from a stream. Significant variation in the incidence of clinical episodes of malaria was observed over small distances. Our results support previous studies conducted in urban and peri-urban areas of Africa suggesting that malaria risk is heterogeneous over small geographic areas and is highest near mosquito breeding sites.4-6

In a rural area of The Gambia, children who lived near mosquito breeding sites had a higher parasite prevalence, but lower likelihood of clinical illness upon infection, compared with children who lived farther from breeding sites; this is likely due to greater antimalarial immunity.8 At the lower levels of transmission typically seen in urban environments, the relative importance of immunity in affording protection against clinical illness may be less than in rural areas.9 Our data and other studies suggest that reducing exposure in urban settings significantly reduces the risk of clinical illness.5,6

With the spread of antimalarial drug resistance, control of malaria in Africa can no longer rely solely on chemotherapy and effective case management. An integrated approach, in-

### Table 1

<table>
<thead>
<tr>
<th>Geographic variable</th>
<th>Number of children</th>
<th>Number of new episodes of symptomatic malaria*</th>
<th>Time at risk (days)</th>
<th>Incidence density (per person year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distance from swamp (meters)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥100</td>
<td>88</td>
<td>32</td>
<td>28,518</td>
<td>0.41</td>
</tr>
<tr>
<td>1–100</td>
<td>44</td>
<td>39</td>
<td>13,919</td>
<td>1.02</td>
</tr>
<tr>
<td>0</td>
<td>173</td>
<td>296</td>
<td>48,738</td>
<td>2.22</td>
</tr>
<tr>
<td>Distance from stream (meters)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥500</td>
<td>72</td>
<td>38</td>
<td>22,814</td>
<td>0.61</td>
</tr>
<tr>
<td>&lt;500</td>
<td>233</td>
<td>329</td>
<td>68,361</td>
<td>1.76</td>
</tr>
</tbody>
</table>

* First and subsequent episodes of malaria classified as new infections using genotyping.

### Table 2

Multivariate analysis of associations between geography and incidence of clinical episodes of malaria*.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Comparison groups</th>
<th>IRR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distance from swamp (meters)</td>
<td>1–100 vs. &gt;100 0 vs. &gt;100</td>
<td>2.4</td>
<td>1.2–4.7</td>
<td>0.01</td>
</tr>
<tr>
<td>Distance from stream (meters)</td>
<td>&lt;500 vs. ≥500 0 vs. &gt;100</td>
<td>1.9</td>
<td>1.2–3.1</td>
<td>0.008</td>
</tr>
</tbody>
</table>

* IRR = incidence rate ratio controlling for age, use of preventive measures (none vs. use of bed nets or chemoprophylaxis), and primary source of water (open spring or well vs. closed tap); and clustering of clinical episodes of malaria for participants living in the same household. CI = confidence interval.
cluding vector control strategies, will be necessary to reduce malaria-associated morbidity and mortality.\textsuperscript{12} Urban areas, with dense population and easily located mosquito breeding sites, may be prime targets for antimalarial control activities.\textsuperscript{3} Identifying areas at highest malaria risk may allow for more efficient targeting of vector control methods, including use of insecticide treated nets, house spraying, larvicide application, and elimination of breeding sites.

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Authors’ addresses: Sarah G. Staedke, E. Willis Nottingham, Philip J. Rosenthal, Grant Dorsey, Department of Medicine, University of California, San Francisco, San Francisco, CA 94143. Jonathan Cox, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, United Kingdom. Moses R. Kamya, Makerere University Medical School, Kampala, Uganda.

Reprint requests: Philip J. Rosenthal, Department of Medicine, University of California, San Francisco, Box 0811, San Francisco, CA 94143, Telephone: 415-206-8845, Fax: 415-648-8425, E-mail: rosnthl@itsa.ucsf.edu.

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