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COMPUTER-BASED MODELING IN SUPPORT OF GLOBAL ERADICATION OF INFECTIOUS DISEASES

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Malaria and polio are current targets of Global Eradication campaigns, and success of these campaigns and any future disease eradication campaigns will provide lasting benefits to humanity. Modern computing and modeling can assist rational planning of disease eradication campaigns to maximize the probability of success in the face of significant challenges and obstacles. We present a new computational framework which is designed to answer questions posed by Eradication campaigns with specific focus on malaria as an example. New detailed models for single malaria infections and mosquito population dynamics are developed and integrated into a large spatial-scale dynamic simulation. The single malaria infection model includes detailed descriptions of parasite intrahost development and human immunology which combine to provide mechanistic explanations of phenomena such as infection duration and adapted response to re-infection. The model for mosquito population dynamics captures the effects of multiple simultaneous vector control interventions upon the mosquito population and the resulting change in parasite population dynamics. The integration of these detailed micro-models into a large-scale spatial simulation with individual resolution allows study of many possible combined-intervention malaria eradication campaigns. Overall probability of campaign success for different combined approaches in the presence of systemic, campaign, and model uncertainty is studied and conclusions for locally-tailored approaches are discussed.

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ENVIRONMENTAL PRESSURE ON THE ANTIBODY RESPONSE TO A CHILDHOOD VACCINE IN NORTHERN SENEGAL

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Environmental factors play a role in vaccine induced immunity. Season-dependent elements have particularly been involved in the modulation of immune responses in developing countries. In Senegal, a sub-Saharan country with two distinct seasons, a dry and a wet one, we conducted a study to investigate whether there is a modulation of the immune response to a childhood vaccine according to seasonal factors. Whooping cough is a vaccine-preventable respiratory disease caused by *Bordetella pertussis* infection, against which Senegalese children are immunized with the Diphteria-Tetanus-whole Pertussis vaccine (DTwP). To assess the level of immunization against whooping cough, we conducted a cross sectional and longitudinal study (1.5 year) in which serum samples were collected from 410 children aged 1 to 10 from 5 villages in Northern Senegal. We tested these sera for antibodies (Ab) against two major antigens of *B. pertussis*: filamentous hemagglutinin (FHA) and pertussis toxin (PT). Although most children were immunized with DTwP, FHA-specific IgG response was significantly different according to age. Until the age of 5, response to FHA was low, and got higher in the older group. Assessment of anti-PT IgG response suggested evidence of recent exposures to the pathogen. Moreover, IgGs to another antigen included in the DTwP vaccine, the tetanus toxoid (TT), was quantified. A high specific Ab response, which decreased with age, was observed. This suggests that the detected low levels of FHA-specific Ab, especially in the younger group of children, were not due to a failure in vaccination. Noteworthily, significant differences in the specific Ab responses to FHA, PT and TT were observed between villages in the same studied area. Besides, when the results from sera collected every three months were compared, a strong effect of seasonal factors on the Ab response to DTwP antigens was detected. The results of this work should be critical in the scope of a better understanding of the role of environmental factors on the establishment and maintenance of immunity to vaccines.

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MALARIA INCIDENCE AND PREVALENCE AMONG CHILDREN LIVING IN A PERI-URBAN AREA ON THE COAST OF BENIN, WEST AFRICA: A LONGITUDINAL STUDY

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Clinical malaria incidence was determined over 18 months in a cohort of 553 children living in a peri-urban area near Cotonou. Three cross-sectional surveys were also carried out. Malaria incidence showed a marked seasonal distribution with 2 peaks, the first corresponding to the long rainy season and the second to the overflowing of Lake Nokoue. The overall *Plasmodium falciparum* incidence rate was estimated at 84/1,000 person-months, its prevalence at over 40% in the two first surveys and 68.9% in the third. Multivariate analysis showed that girls and people living in closed houses had a lower risk of clinical malaria. Bed net use was associated with a lower risk of malaria infection. Conversely, children of families owing a pirogue were at higher risk of clinical malaria. Considering the high pyrethroids resistance, indoor residual spraying with either a carbamate or an organophospate insecticide may have a major impact on the malaria burden.

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COMBINED UTILITY OF TOURNIQUET TEST AND WHITE BLOOD CELL COUNT AS TRIAGE CRITERIA FOR DENGUE IN THE AMERICAS

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As the clinical presentation of dengue can be non-specific, and rapid diagnostic tests are not readily available, finding easily obtainable markers that can distinguish dengue from other acute febrile illnesses is a priority. Data from Thailand suggests that the combination of a positive tourniquet test (TT) and leukopenia can distinguish dengue from other febrile illnesses in children; little data exists on the utility of these tests in adults or in the Americas. We evaluated the utility of the TT and leukopenia (white blood cell count <4000/mm^3) for identifying dengue as part of a febrile illness surveillance study conducted in the Emergency Department of the Hospital San Lucas in Ponce, Puerto Rico. From September to December 2009, 284 patients presenting to the ED with fever for 2-7 days and no identified source of infection were enrolled. Participants were tested for influenza, dengue, leptospirosis, and enteroviruses. Thirty-one (10.9%) of patients were confirmed as having dengue; a definitive etiology was determined for 142 others (136 influenza, 2 leptospirosis, 3 enterovirus) and 111 patients had no infectious etiology identified. Fifty-two percent of laboratory-positive dengue cases had a positive TT versus 18% of