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ABSTRACT BOOK

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1.4 million premises respectively. The PTF was reactivated in 2017 and 24 PTF meetings have been conducted to date to assess the progress of control activities with the participation of relevant stakeholders. In-service training programmes were conducted (35 and 15 in 2017 and 2018 respectively) for medical doctors and other clinical staff by the local and foreign experts on clinical management. Moreover, the capacities of high dependency units were strengthened to manage Dengue patients efficiently. During SMCC's conducted in 2017 and 2018, health workers along with the Tri-Forces/Police found 20% and 21% potential breeding places and 1.98% and 2.29% positive breeding places in the respective years. Thus there was a reduction in the incidence of Dengue from 865.9 to 239.8 per 100,000 population (in 2017 and 2018 respectively) and case fatality rate has been halved from 0.24% to 0.11% from 2017 to 2018. An integrated approach is an effective method in sustaining low endemicity and curtailing Dengue outbreaks.

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COMPARING THE COMPETENCE OF GHANAIAN AND VIETNAMESE *AEDES* MOSQUITOES AS VECTORS OF THE DENGUE VIRUS

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Dengue fever is an arboviral infection of public health concern caused by at least 4 antigenically different serotypes of the dengue virus. It is transmitted by the *Aedes* mosquito, infecting 390 million people annually with 25,000 deaths. The distribution, frequency and intensity of outbreaks have varied quite significantly over the years. In 2016, the Americas and Asia reported cases in the millions and hundreds of thousands respectively while Africa reported cases in the thousands. Within Africa, Ghana, unlike her neighboring countries, is yet to report a single outbreak despite an abundance of the *Aedes* mosquito vector. Serological reports have however suggested possible exposure to the dengue virus or a closely related flavivirus. While many factors have been hypothesized as the reason for the differences, determining the effect of vector competence is of utmost importance. The aim of this study was therefore to compare the vector competence of *Aedes* mosquitoes from Ghana and dengue endemic Vietnam. In this study, Mosquito larvae were collected from various parts of Ghana and Vietnam and established in the lab. The virome of the laboratory colonies were determined after which adult female mosquitoes were infected with the dengue virus. The Saliva, thorax/abdomen and carcass of individual mosquitoes were harvested and screened at 7 and 14 days post infection. The infection rate, dissemination rate and transmission rate were determined by qPCR and Focus assay. Our results show Vietnamese *Aedes* mosquitoes to be significantly more susceptible to Dengue virus colonization. Furthermore the dissemination rate of the virus in the Vietnamese mosquitoes was double that of the Ghanaian mosquitoes. Last but not least while there was no significant difference in the time viruses were detected in the saliva of infected mosquitoes, the concentration in the Vietnamese mosquitoes were significantly higher. In conclusion, *Aedes* mosquitoes from Vietnam are more efficient vectors of the Dengue virus than *Aedes* mosquitoes from Ghana and the difference in vector competence may play a significant role in distribution and intensity of outbreaks.

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CONGENTITAL DENGUE: CD133+ AND CD34+ HEMATOPOETIC STEM CELLS IN UMBILICAL CORD BLOOD ARE INFECTABLE BY DENGUE VIRUS CONFERRING VERTICAL TRANSMISSION

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Dengue affects more than 100 million people worldwide annually. Numerous routes of transmission for dengue virus (DENV) have been documented. The cases of dengue resulting from stem cell transplantations and mother-to-infant vertical transmission are escalating in recent years. Consequences of mother-to-fetal transmission have been shown to be associated with miscarriage and stillbirth. DENV proteins and genomic RNA have been detected in placenta, serum and cord blood of baby with a fever and subclinical infection upon delivery. Umbilical cord blood (UCB) is the essential bridge connecting placenta and infant and is abundant with stem cells. We, therefore, hypothesize that DENV after passing through placenta may amplify further in stem cells within UCB. In this study, freshly obtained UCBs were utilized and fluorescence-activated cell sorting (FACS) was performed to analyze the stem cells after DENV infection. Viral titers in supernatants of infected UCB were performed by plaque assay. Results showed that cells in UCB were highly permissive to DENV, enhanced proliferation of hematopoietic stem and progenitor cells (HSPC) was observed, balance of transcriptional factors (GATA-1,GATA-2,GATA-3) were disturbed, DENV nonstructural protein 1 (NS1) was mainly associated with CD34+ and/or CD133+ cells analyzed by FACS and immunofluorescence staining, sorted CD133+ or CD34+ cells were infectable by DENV, and infectious DENV could be recovered from infected CD34+ and CD133+ cells upon co-culture . Furthermore, viral RNA in specific organelle was found after 30 days of infection, suggesting the longevity of stem cells in DENV infected UCB. Our cumulative results submit that CD133+ and/or CD34+ cells in UCB are not only permissive to DENV infection but also might serve as a reservoir for dissemination of the virus. The findings may indicate the unique property of DENV in stem cells contributing to DENV transmission from mother-to-infant, resulting in the clinical significances in newborn babies, especially in dengue-endemic regions.

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DENGUE FEVER, *AEDES AEGYPTI* AND CLIMATE DYNAMICS FROM THE TEMPERATE CITY OF CÓRDOBA, ARGENTINA, DURING THE TIME SERIES OF 2009-2017

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Argentina is located at the southern range of arboviral transmission by *Aedes aegypti* and has experienced a rapid increase in arbovirus transmission in recent years. The aim of this study was to present, for the first time, the methods and findings from a prospective long-term entomological surveillance study that began in 2009 in the city of Córdoba, following the first dengue virus (DENV) outbreak. We analyze the seasonal and interannual dynamics of DENV transmission in the city,

in relation to *Ae. aegypti* indices and local climate. Therefore, from 2009 to 2017, larval surveys were conducted monthly, from November to May, in 600 randomly selected households distributed across the city. From 2009 to 2013, ovitraps (n=177) were sampled weekly to monitor the oviposition activity of *Ae. aegypti*. Cross correlation analysis was used to identify significant lag periods between climate, entomologic and epidemiologic variables. Climate, entomologic and epidemiologic variables exhibited a strong seasonal pattern with a single peak within the year (climate, epidemiologic) or sampling period (entomologic). The largest correlation between autochthonous dengue and minimum temperature was at 9 weeks (positive), and there was a large positive correlation between autochthonous dengue and relative humidity (minimum, mean, maximum) at 4 weeks. There was a positive correlation with mean relative humidity at lag 4 in 2009, and a negative correlation between ovitrap positivity and minimum relative humidity at lag 2 in 2010. Ovitrap positivity was positively correlated with relative humidity (mean, maximum) and precipitation at a 5-week lag and negatively correlated with mean temperature in 2012. This prospective entomological surveillance study provides the first evidence that *Ae. aegypti* larval indices in this temperate region have increased over the last 9 years, a period when arboviral diseases have become epidemic for the first time. These findings suggest an increasing the risk of arbovirus emergence and sustained transmission at temperate southern latitudes, where these diseases were not previously reported.

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UNCOVERING THE DENGUE-1 SPECIFIC MEMORY B CELL DERIVED ANTIBODY REPERTOIRE IN IMMUNE DONORS 1 TO 43 YEARS AFTER DENGUE INFECTION IN A NON-ENDEMIC COHORT

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Mosquito transmitted flaviviruses, including dengue virus (DENV) are among the most important vector-borne pathogens of humans worldwide, responsible for 100 million symptomatic cases and ~35,000 deaths *each* year. Upon DENV infection, DENV-specific host B-cells differentiate and proliferate. Some become long-lived antibody-secreting cells (long-lived plasma cells) while others become DENV-specific memory B cells (MBCs) that remain in circulation, poised to protect against future infections, forming a founder population that plays a critical role in establishing and maintaining long-term viral immunity. Despite this critical role, much remains incompletely described regarding lifespan, specificity, and the potency and breadth of MBCs and the antibodies they encode and secrete upon reinfection. This knowledge is vital for understanding long-term human immunity to flaviviruses as well as for rational vaccine design. Here we identify and quantify DENV-specific MBCs in humans with a single DENV infection. Using PBMCs from 15 primary DENV-1 donors with times since infection ranging from 1-43 years, we employed two complimentary experimental approaches to quantify DENV-specific MBCs. In our first approach, PBMCs were stimulated *in vitro* to become antibody-secreting cells and the resulting antibodies assessed for DENV-specificity by ELISA using whole DENV virus (DENV1-4) as well as non-structural protein NS1. The second method used flow cytometry to quantify human MBCs (CD3-CD14-CD19+CD27+IgD-) that bind fluorescently labeled DENV. Using these approaches, we were able to identify DENV-specific MBCs that remain in circulation decades after infection. MBC frequency was inversely correlated with time since infection. These experiments lay the foundation to functionally characterize DENV-specific MBCs and the antibodies they are programmed to secrete, including frequency of DENV-binding and neutralizing MBCs and the potency and breadth these antibodies have against antigenically diverse DENV. The results of this project will provide insight into the MBC founder population and the role it plays in broader DENV immunity.

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CHARACTERIZING THE SPATIO-TEMPORAL DYNAMICS OF DENGUE IN BRAZIL

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Roughly half of the global population is at risk of dengue infection, predominantly in urban areas in Southeast Asia and Latin America. There are four main serotypes of dengue virus that co-exist, and infection confers long-term immunity against only the infecting serotype. Although dengue is classically considered a childhood disease, the age distribution of cases depends on local demography as well as how long serotypes have been present. In Brazil, where dengue was re-introduced in the 1980s and which now accounts for the majority of dengue cases reported in the Americas, the disease classically affected mainly adult populations. However, in 2007, the age distribution of cases drastically shifted towards younger age groups. Here, we investigate the causes and consequences of this punctuated drop in the age distribution of dengue cases, leveraging annual state-level counts of age-stratified, hospitalized dengue cases in Brazil between 1992 and 2017. We deploy a mathematical modeling framework to clarify spatio-temporal patterns of population-level susceptibility to dengue in Brazil, and explore the interplay between human demography, transmission epidemiology, and serotype-specific immunity on dengue burden more generally. With more countries prone to dengue transmission undergoing the demographic transition, the ability to project age-structured cases into the future will inform public health planning. Clarifying serotype-specific immunity and risk will also be important for countries considering introduction of childhood immunization with the dengue vaccine.

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THE LABORATORY PROFILE OF DENGUE IN PATIENTS ADMITTED TO TEACHING HOSPITAL ANURADHAPURA

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Dengue is an arthropod-borne viral disease caused by an RNA virus belonging to the genus Flaviviruses. Dengue has become a major public health problem in the world as well as in Sri Lanka. The clinical and laboratory profiles of dengue may vary depending on the age, immunity states and the involved serotype of the virus etc. Nevertheless, the differences of presentation, the timely diagnosis, triage, and proper monitoring plays a vital role in saving lives of dengue patients. For this, the knowledge on clinical presentations, the utility of the available national and international guidelines and the choice of ideal lab test/s for the confirmation, in the local context, should be available to the clinicians and other stakeholders. This study was aimed to assess the utility of specific laboratory tests for the correct diagnosis of dengue. The data on available investigation results and blood samples were collected from patients admitted to medical wards of Teaching Hospital Anuradhapura, with the probable diagnosis of dengue. The PCR testing was conducted in the PCR laboratory at the Department of Veterinary Pathobiology, University of Peradeniya, during one year starting from 1st December 2016. A total of 213 patients were recruited by convenient sampling. The mean age of the study group was 32.98 years (SD=13.1). Of them, the majority (81.7%) were males. Only 1.6 % of the patients have a maximum drop of more than 100 x 10^3 per mm^3 platelets per one day. RT PCR was positive only in 38 blood samples. The sensitivity and specificity of NS1 and/or Ig M dengue 44.7% and 65.7% respectively. The commonest serotype was DENV 2. The utility of serology, NS1 and, PCR and virus isolation tests in the diagnosis of the disease in the Sri Lankan context should be investigated further by researchers.