define the species-level classification of this group of tick-borne orbiviruses includes pairwise co-infection of Bukakata, Fomede, and Chobar Gorge followed by serial passage on IDE8 cells (derived from *Ixodes scapularis*), Vero cells, and R06E cells (derived from *Rousettus aegyptiacus* bats). Plaque purification of isolates following serial passage will be analyzed for the occurrence of segmental reassortment utilizing RT-PCR and Sanger sequencing. Analysis of reassortment potential in cell lines derived from both the purported host and arthropod vector species will provide unique and valuable information to the study of orbivirus speciation.

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SENSITIVITY OF A RAPID DIAGNOSTIC TEST FOR INFLUENZA

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Influenza causes considerable morbidity and has significant operational impact in the military. Rapid influenza diagnostic tests (RDTs) which detect viral antigens of influenza are used as tools to screen patients with suspected influenza and are used to reduce inappropriate antibiotic use, decrease unnecessary diagnostic testing and to facilitate timely control measures prior to results of confirmatory tests during outbreaks or during field deployments where access to confirmatory tests is unavailable. Between Aug 2011 to Oct 2016, patients presenting with influenza-like illness (ILI) (n=2,333) at the V Luna Medical Center, Quezon City, Philippines were tested using Quickvue (QV) influenza A+B RDT and influenza real-time RT-PCR. Statistical tests of association were done to determine effect of age, viral titers (Ct values), and timing of collection on QV sensitivity/specificity to detect different influenza sub-types (Flu A/H3, Flu A/pdmH1, Flu A/H3+Flu A/pdmH1and Flu B). P value <0.05 was considered statistically significant. QV sensitivity, specificity, positive and negative predictive values can be seen in Table 1. Linear regression showed that QV sensitivity across all sub-types was significantly correlated with lower Ct values (higher virus titers) (p<0.001) and except for Flu A/H3 (p=0.974), was also significantly associated with timing of specimen collection (p<0.05). There were no statistically significant difference noted in QV sensitivity for Flu A/H3 (p=0.130), pandemic H1/N1 (p=0.207), Flu A/H3+pandemic H1/N1 (p=0.341), and Flu B (p=0.103) across different age groups but sensitivity of QV significantly differed (p<0.001) across the different influenza sub-types. The findings highlight the need to develop more sensitive influenza RDTs to detect circulating influenza strains.

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SPATIAL AND TEMPORAL SPREAD OF ZIKA AND CHIKUNGUNYA VIRUSES IN COLOMBIA, A GRAVITY-MODEL BASED APPROACH

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Zika virus (ZIKV) and chikungunya virus (CHIKV) were recently introduced into the Americas resulting in significant disease burdens. Understanding the spatial and temporal dynamics of the recent outbreaks in Colombia is key to informing control strategies at the subnational level. We have analyzed anonymized line lists data on 100,000 ZIKV and 380,000 CHIKV cases reported to SIVIGILA, Colombia's national public health surveillance system, between 2014 and 2017. These data include both suspected and laboratory confirmed cases. We fitted gravity models to analyze transmission between cities based on population size and distance, utilizing the approach of Eggo et al. in their study of the 1918 influenza pandemic. We were able to track the spread of reported cases between more than 300 locations (administrative level 2) on a weekly basis. We assessed the extent to which transmission depended on population density and then examined the effects of altitude, temperature, and annual precipitation on ZIKV and CHIKV spread. These environmental factors affect mosquito development and could help explain observed disease trends. Modeling at such fine spatial scale will inform both surveillance and control strategies.

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ASSESSMENT OF POLIOVIRUS ANTIBODY SEROPREVALENCE IN HIGH RISK AREAS FOR VACCINE-DERIVED POLIOVIRUS TRANSMISSION IN MADAGASCAR

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Vaccine-derived polioviruses (VDPV) outbreaks typically occur in areas of low poliovirus immunity. Madagascar successfully eradicated wild poliovirus in 1997. However, multiple VDPV outbreaks have occurred since then, and numerous vaccination campaigns have been carried out to control the VDPV outbreaks. We conducted a survey of poliovirus neutralizing antibodies among Malagasy children to assess the performance of vaccination campaigns and to estimate the risk of future VDPV outbreaks. A random community survey was undertaken in children aged 6-11 months, 36-59 months and 5-14 years of age in four high-risk areas of Madagascar (Mahajanga, Toliara, Antsalova, and Midongy-atsimo) and in a reference area (Antananarivo). After obtaining informed consent, basic demographic and vaccination history, 2 mL of peripheral blood were collected. Neutralizing antibodies against all three poliovirus serotypes 1, 2, 3 (PV1, PV2, PV3 respectively) were detected by using a standard microneutralization assay. There were 1500 children enrolled and 1496 (>99%) provided sufficient quantity of blood for analysis. Seroprevalence for PV1 was >90% in all age groups and the study areas. PV2 seroprevalence ranged between 75-100% with the lowest found in the youngest age group in Midongy and Toliara. PV3 seroprevalence ranged between 79-100%. The seroprevalences in the reference area was not significantly different from that of high risk areas. Madagascar achieved high population immunity. In order to sustain the protection, routine immunization needs to be strengthened. Currently, the risk of new VDPV emergences in Madagascar appears low.

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CLINICAL DEVELOPMENT OF VIRAL VECTORED VACCINES AGAINST MERS-COV

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Viral vectors have been used as delivery platforms for vaccines against several pathogens including malaria, HIV, TB, influenza, Ebola and hepatitis and have demonstrated acceptable reactogenicity in all age-groups including neonates, as well as excellent immunogenicity. Of seven vaccine candidates in clinical development against ebolavirus disease (EVD) during the recent West African outbreak, six were based on viral vectored technology with rVSV-ZEBOV demonstrating high, short-term efficacy against disease in a Phase III ring vaccination study in Guinea. Chimpanzee adenoviruses (ChAd) are attractive as viral vectors due to ease of genetic manipulation, compatibility with high-yielding GMP production processes, a safety profile suitable for administration to infants as young as 1-week of age and induction of potent cell-mediated immunity and neutralising

antibody responses. Building on these features, we are undertaking clinical development of a number of vaccines against important outbreak pathogens identified by the WHO Blueprint for R&D preparedness. Using ChAd vectors, the Jenner Institute is currently evaluating vaccine candidates against CCHF, EVD and Marburg, Lassa Fever and Nipah in pre-clinical models. Vaccines against MERS-CoV, Rift Valley Fever, Chikungunya and Zika will enter Phase I clinical trials during 2018 and early 2019. MERS-CoV is a zoonotic virus that causes respiratory infection and severe disease in humans with a fatality rate as high as 35%. Camels are the animal reservoir for the virus and hence a vaccine with utility in both dromedaries and humans would be of significant public health benefit. We will present safety and immunogenicity data from this Phase I, dose-escalation, first-in-man trial of ChAdOx1 MERS describing humoral and cellular immune responses from the study, which started in March 2018. A second Phase I trial will begin in Saudi Arabia in late 2018. This reinforces the utility of ChAd vectors as vaccines for outbreak pathogens because of the capability to rapidly produce GMP vaccine stockpiles for pandemic preparedness.

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OXIDATIVE STRESS IN MALARIA ENDOTHELIAL PATHOLOGY

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Malaria remains a global burden worldwide, causing approximately 400,000 deaths annually. Blood stage malaria is characterized by a strong inflammatory response and also considered to be highly oxidative. Recent work in our laboratory indicates that oxidative stress could be an important driver of inflammation in malaria. In particular, we have found the host enzyme xanthine oxidase (XO) in combination with *Plasmodium falciparum*-infected erythrocytes induces a strong inflammatory response in human monocyte-derived macrophages. XO is an enzyme involved in purine catabolism, but is most noted for its ability to produce reactive oxygen species (ROS). XO has been shown to be elevated in African children with malaria and we have also found elevated activity of XO in adult Indian patients with uncomplicated or cerebral malaria. To further investigate the role of oxidative stress and disease pathology, precisely the role of XO in cerebral malaria, we studied the effects of XO alone on human brain microvascular endothelial cells (HBMECs). When we incubated HBMECs with XO, we observed a disruption in endothelial cell junctions. We will study the role of oxidative stress in cerebral malaria further by determining the effects of XO in combination with *P. falciparum*-infected erythrocytes on HBMECs and the signaling involved. Using mice models of malaria, we will also determine whether XO binds the endothelium during malaria infection, as described when this enzyme is in the circulation. Through these investigations we hope to obtain a better understanding of the interplay between oxidative stress and malaria endothelial pathology.

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ASSESSMENT OF ARTEMISININ COMBINATION REPEATED TREATMENT EFFECT ON BLOOD CELL LINES PARAMETERS DURING A TWO-YEAR FOLLOW UP INVOLVING 3ACT, ARTESUNATE-PYRONARIDINE (PYR), DIHYDROARTEMININ-PIPERAQUINE (DHA-PQ) COMPARED TO ARTESUNATE-AMODIAQUINE (ASAQ) IN THE TREATMENT OF THE UNCOMPLICATED ACUTE *PLASMODIUM FALCIPARUM* MALARIA CASES IN BANFORA HEALTH DISTRICT

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Artemisinin combination therapies (ACTs) still remains in Sub Saharan Africa, the most effective anti-malarial drugs for the malaria treatment in areas with multidrug resistant *Plasmodium falciparum* malaria. The use of these drugs to treat malaria may be associated with possible side effects on the blood cells. It was therefore the aim of this study to undertake a comparative effect of a repeatedly administration of artesunate-amodiaquine, dihydroartemisinine-piperaquine, and artesunate-pyronaridine on haematological parameters (RBC count, Hb, WBC count, Platelets count) in *P. falciparum* uncomplicated malaria patients living in Burkina Faso. Confirmed malaria infected patients (n=763) aged from 6months to 54 years of both sexes were included in the study carried out in Banfora Health District area in Burkina Faso. About 2ml of blood sample was collected into EDTA tube from the same patient before the ACT administration and after at day 3, 7 and 28 of the follow up for blood cell lines analysis at each malaria episode. The findings of this present study show that Artesunate-Amodiaquine, Dihydroartemisinine-Piperaquine and Pyronaridine-Artesunate have effects on the hematological parameters in *P. falciparum* malaria infected patients. The three ACTs significantly reduced the proportion of abnormal blood levels of white blood cells, neutrophils, eosinophils and lymphocytes without significant effects on the proportion on the abnormal level of basophils cell. The proportion of abnormal blood level of RBC, hb and platelets were significantly increased at the day 3 after treatment before decreasing at day 28. However a repeatedly treatment of these three ACTs had no significantly effect on the blood cell level.

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DEVELOPMENT OF RELIABLE MOSQUITO INFECTIONS WITH EAST AFRICAN *PLASMODIUM FALCIPARUM* STRAINS FOR HETEROLOGOUS CONTROLLED HUMAN MALARIA INFECTION

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Since 1985, the Walter Reed Army Institute of Research (WRAIR) has produced *P. falciparum*-infected mosquitoes for use in clinical trials to evaluate anti-malarial vaccines, drugs, and immunity. The vast majority of those &gt 110 experimental malaria challenges used Pf3D7 and its parent strain, PfNF54, but the recent progression of candidate anti-malarial products necessitates development of *P. falciparum* strains that are heterologous to Pf3D7. The standard methodology used to grow PfNF54 is insufficient to produce sporozoite infections with most other *P. falciparum* strains, therefore new methodology must be formulated to support heterologous strain production. In a multi-laboratory effort, the capabilities and resources of WRAIR and USAMRD-Kenya combine to form a *P. falciparum* development pipeline which has led to the advancement