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David Musoke, George Miiro, George Karani, Keith Morris, Jessica Nakiyingi-Miiro, Simon Kasasa, David Guwatudde, Miph Boses Musoke. Promising perceptions, divergent practices and barriers to integrated malaria prevention in Wakiso District, Uganda: A mixed methods study. PLoS ONE 10(4): e0122699. doi:10.1371/journal.pone.0122699

BACKGROUND: The World Health Organization recommends use of multiple approaches to control malaria. The integrated approach to malaria prevention advocates the use of several malaria prevention methods in a holistic manner. This study assessed perceptions and practices on integrated malaria prevention in Wakiso district, Uganda.

METHODS: A clustered cross-sectional survey was conducted among 727 households from 29 villages using both quantitative and qualitative methods. Assessment was done on awareness of various malaria prevention methods, potential for use of the methods in a holistic manner, and reasons for dislike of certain methods. Households were classified as using integrated malaria prevention if they used at least two methods. Logistic regression was used to test for factors associated with the use of integrated malaria prevention while adjusting for clustering within villages.

RESULTS: Participants knew of the various malaria prevention methods in the integrated approach including use of insecticide treated nets (97.5%), removing mosquito breeding sites (89.1%), clearing overgrown vegetation near houses (97.9%), and closing windows and doors early in the evenings (96.4%). If trained, most participants (68.6%) would use all the suggested malaria prevention methods of the integrated approach. Among those who would not use all methods, the main reasons given were there being too many (70.2%) and cost (32.0%). Only 33.0% households were using the integrated approach to prevent malaria. Use of integrated malaria prevention by households was associated with reading newspapers (AOR 0.34; 95% CI 0.22 -0.53) and ownership of a motorcycle/car (AOR 1.75; 95% CI 1.03 - 2.98).

CONCLUSION: Although knowledge of malaria prevention methods was high and perceptions on the integrated approach promising, practices on integrated malaria prevention was relatively low. The use of the integrated approach can be improved by promoting use of multiple malaria prevention methods through various communication channels such as mass media.

Bobbi Fleiss, Cally Tann, Vincent Degos, Stéphanie Sigaut, Juliette Van Steenwinckel, Anne-Laure Schang, Anton Kichev, Nicola J Robertson, Carina Mallard, Henrik Hagberg, Pierre Gressen Inflammation-induced sensitisation of the term infant brain. Developmental medicine and child neurology Volume 57, Issue Supplement S3, pages 17–28, April 2015. DOI: 10.1111/dmcn.12723

Perinatal insults are a leading cause of infant mortality and amongst survivors are frequently associated with neurocognitive impairment, cerebral palsy (CP), and seizure disorders. The events leading to perinatal brain injury are multifactorial. This review describes how one subinjurious factor affecting the brain sensitizes it to a second injurious factor, causing an exacerbated injurious cascade. We will review the clinical and experimental evidence, including observations of high rates of maternal and fetal infections in term-born infants with neonatal encephalopathy and cerebral palsy. In addition, we will discuss preclinical evidence for the sensitizing effects of inflammation on injuries, such as hypoxia-ischaemia, our current understanding of the mechanisms underpinning the sensitization process, and the possibility for neuroprotection.

Prentice S, Webb E, Dockrell H, Kaleebu P, Elliott A, Cose S. The non-specific effects of BCG vaccination on the innate immune system: study protocol for an investigator-blinded, randomised controlled trial comparing BCG vaccination at birth to at 6 weeks of age in Ugandan infants. Trials. doi:10.1186/s13063-015-0682-5

BACKGROUND: The potential for Bacillus Calmette-Guérin (BCG) vaccination to protect infants against non-mycobacterial disease has been suggested by a randomised controlled trial conducted in low birth-weight infants in West Africa. Trials to confirm these findings in healthy term infants, and in a non-West African setting, have not yet been carried out. In addition, a biological mechanism to explain such heterologous effects of BCG in the neonatal period has not been confirmed. This trial aims to address these issues by evaluating whether BCG non-specifically enhances the innate immune system in term Ugandan neonates, leading to increased protection from a variety of infectious diseases.

METHODS: This trial will be an investigator-blinded, randomised controlled trial of 560 Ugandan neonates, comparing those receiving BCG at birth with those receiving BCG at 6 weeks of age. This design allows comparison of outcomes between BCG-vaccinated and -naïve infants until 6 weeks of age, and between early and delayed BCG-vaccinated infants from 6 weeks of age onwards. The primary outcomes of the study will be a panel of innate immune parameters. Secondary outcomes will include clinical illness measures.

DISCUSSION: Investigation of the possible broadly protective effects of neonatal BCG immunisation, and the optimal vaccination timing to produce these effects, could have profound implications for public healthcare policy. Evidence of protection against heterologous pathogens would underscore the importance of prioritising BCG administration in a timely manner for all infants, provide advocacy against the termination of BCG's use and support novel anti-tuberculous vaccine strategies that would safeguard such beneficial effects.

Soo-Yon Rhee, Jose Luis Blanco, Michael R. Jordan, Jonathan Taylor, Philippe Lemey, et al (Deogratius Ssemwanga). Geographic and Temporal Trends in the Molecular Epidemiology and Genetic Mechanisms of Transmitted HIV-1 Drug Resistance. Plos Medicine 2015 DOI: 10.1371/journal.pmed.1001810

BACKGROUND: Regional and subtype-specific mutational patterns of HIV-1 transmitted drug resistance (TDR) are essential for informing first-line antiretroviral (ARV) therapy guidelines and designing diagnostic assays for use in regions where standard genotypic resistance testing is not affordable. We sought to understand the molecular epidemiology of TDR and to identify the HIV-1 drug-resistance mutations responsible for TDR in different regions and virus subtypes.

METHODS AND FINDINGS: We reviewed all GenBank submissions of HIV-1 reverse transcriptase sequences with or without protease and identified 287 studies published between March 1, 2000, and December 31, 2013, with more than 25 recently or chronically infected ARV-naïve individuals. These studies comprised 50,870 individuals from 111 countries. Each set of study sequences was analyzed for phylogenetic clustering and the presence of 93 surveillance drug-resistance mutations (SDRMs). The median overall TDR prevalence in sub-Saharan Africa (SSA), south/southeast Asia (SSEA), upper-income Asian countries, Latin America/Caribbean, Europe, and North America was 2.8%, 2.9%, 5.6%, 7.6%, 9.4%, and 11.5%, respectively. In SSA, there was a yearly 1.09-fold (95% CI: 1.05-1.14) increase in odds of TDR since national ARV scale-up attributable to an increase in non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance. The odds of NNRTI-associated TDR also increased in Latin America/Caribbean (odds ratio [OR] = 1.16; 95% CI: 1.06-1.25), North America (OR = 1.19; 95% CI: 1.12-1.26), Europe (OR = 1.07; 95% CI: 1.01-1.13), and upper-income Asian countries (OR = 1.33; 95% CI: 1.12-1.55). In SSEA, there was no significant change in the odds of TDR since national ARV scale-up (OR = 0.97; 95% CI: 0.92-1.02). An analysis limited to sequences with mixtures at less than 0.5% of their nucleotide positions-a proxy for recent infection-yielded trends comparable to those obtained using the complete dataset. Four NNRTI SDRMs-K101E, K103N,

Y181C, and G190A-accounted for >80% of NNRTI-associated TDR in all regions and subtypes. Sixteen nucleoside reverse transcriptase inhibitor (NRTI) SDRMs accounted for >69% of NRTI-associated TDR in all regions and subtypes. In SSA and SSEA, 89% of NNRTI SDRMs were associated with high-level resistance to nevirapine or efavirenz, whereas only 27% of NRTI SDRMs were associated with high-level resistance to zidovudine, lamivudine, tenofovir, or abacavir. Of 763 viruses with TDR in SSA and SSEA, 725 (95%) were genetically dissimilar; 38 (5%) formed 19 sequence pairs. Inherent limitations of this study are that some cohorts may not represent the broader regional population and that studies were heterogeneous with respect to duration of infection prior to sampling.

CONCLUSIONS: Most TDR strains in SSA and SSEA arose independently, suggesting that ARV regimens with a high genetic barrier to resistance combined with improved patient adherence may mitigate TDR increases by reducing the generation of new ARV-resistant strains. A small number of NNRTI-resistance mutations were responsible for most cases of high-level resistance, suggesting that inexpensive point-mutation assays to detect these mutations may be useful for pre-therapy screening in regions with high levels of TDR. In the context of a public health approach to ARV therapy, a reliable point-of-care genotypic resistance test could identify which patients should receive standard first-line therapy and which should receive a protease-inhibitor-containing regimen.