ABSTRACTS OF ORAL PRESENTATIONS

OC 8173 RAPID DETECTION OF *MYCOBACTERIUM ULCERANS* BY RECOMBINASE POLYMERASE AMPLIFICATION

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Background There are no primary measures to prevent people from contracting Buruli ulcer, mainly due to poor understanding of its epidemiology. The current control strategy emphasises early diagnosis and prompt treatment, with the goal of avoiding the complications associated with advanced stages of the disease. There is no diagnostic test for the disease appropriate for use at the primary health care level where most cases are detected and treated. Diagnosis based on clinical signs is unreliable in inexperienced hands and complicated by infections that have similar presentations. This study was to develop and evaluate the use of recombinase polymerase amplification (RPA) assay for the detection of *Mycobacterium ulcerans* at the point of patient care.

Methods A specific fragment of IS2404 of *M. ulcerans* was amplified in 15 min at a constant temperature of 42°C, using the RPA assay and analysed on a portable fluorometre. The method was tested for sensitivity and specificity with molecular standard of IS2404 DNA fragment, various *M. ulcerans* strains, other mycobacteria and environmentally associated bacteria. Additionally, the assay performance as a diagnostic tool was tested with archived DNA from symptomatic patients. All results were compared with that of a highly sensitive IS2404 PCR.

Results The detection limit was 50 copies of IS2404 in 15 min using plasmid standard and 125 fg with genomic *Mu* DNA equivalent 25 genomic copies. The assay was highly specific in detecting all strains of *M. ulcerans* with no observed cross reactivity with other mycobacteria and common skin colonising bacteria. The clinical sensitivity and specificity of the BU-RPA assay using clinical samples was 86% and 100% respectively.

Conclusion We have developed a real-time isothermal RPA assay for the detection of *M. ulcerans* as a cheaper alternative to PCR. Combining this assay with a simple extraction protocol will maximise its use as point-of-care test for Buruli ulcer.

OC 8215 DIAGNOSTIC ACCURACY OF XPERT MTB/RIF ULTRA FOR PULMONARY TUBERCULOSIS IN CHILDREN: A MULTICENTRE COMPARATIVE STUDY

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Background Xpert® MTB/RIF (Xpert) has suboptimal sensitivity for the diagnosis of pulmonary tuberculosis in children. The next-generation Xpert MTB/RIF Ultra assay (Xpert Ultra) is substantially more sensitive than Xpert and may allow improved detection of paediatric tuberculosis. We evaluated the diagnostic accuracy of Xpert Ultra versus Xpert in the detection of pulmonary tuberculosis in children.

Methods From May 2011 to September 2012, children with presumptive pulmonary tuberculosis were enrolled at two Tanzanian research sites in the EDCTP-funded TB CHILD project. Sputum samples were collected and examined for tuberculosis using sputum smear, Xpert and culture. Xpert Ultra analysis was performed between January and June 2017 at both sites using decontaminated sputum pellets which had been stored at −80°C. The diagnostic accuracy of Xpert and Xpert Ultra was determined using well-defined case definitions as reference standard.

Results In total, 215 children were included in the analysis. The median age was 5.4 years (IQR, 1.5 to 9.9), the HIV prevalence was 52%, and 28 children (13%) had culture-confirmed pulmonary tuberculosis. When only the first available sample of each patient was considered, the sensitivity of Xpert Ultra was 64.3% (95% CI: 44.1 to 81.4) while that of Xpert was 53.6% (95% CI: 33.9 to 72.5). The specificity of Xpert Ultra based on the analysis of all available samples was 98.1% (95% CI: 93.4 to 99.7), whereas that of Xpert was 100%.

Conclusion In settings with a high burden of tuberculosis and HIV, Xpert Ultra had a better sensitivity than Xpert in children. However, the specificity was slightly lower than that of Xpert. Thus, Xpert Ultra has the potential to increase the reliability and the speed of tuberculosis diagnosis in children.

OC 8244 QUANTITATIVE LATERAL FLOW ASSAY FOR DETECTION OF *M. LEPRAE* INFECTION USING FINGERSTICK BLOOD

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Background Leprosy is a debilitating, infectious disease caused by *Mycobacterium leprae* leading to skin and nerve damage and often lifelong handicaps. The unabated rate of new leprosy case detection indicates that transmission of *M. leprae* is persistent and that current measures for prevention and multidrug therapy (MDT) are insufficient. Contact with *M. leprae*-infected individuals is a risk factor for development of leprosy. Thus, detection of *M. leprae*-infected individuals without clinical symptoms, allowing informed decision making on who needs treatment at a preclinical stage, is vital to interrupt transmission and can help prevent leprosy.

Immunoprophylaxis by vaccination or post-exposure prophylaxis (PEP) with antibiotics provide effective strategies for the prevention of leprosy. To target individuals unknowingly spreading leprosy bacilli, methods allowing objective measurement of *M. leprae* infection are needed. Besides antibody (Ab) levels that correspond with bacterial load and higher risk of progression to leprosy, detection of cytokine profiles can provide significant added value to identify infection.

Methods Quantitative detection of anti-PGL-I IgM antibodies, and cytokines such as IP-10 was performed on lateral flow (LF) test strips utilising the luminescent up-converting particle (UCP) technology. Precise amounts of fingerstick (FS)-blood samples were collected using disposable heparinised capillaries.

Ab and cytokine levels in both FS-blood and serum from leprosy patients in South-Africa, Brazil, Bangladesh and the Netherlands and (their) contacts were measured using a portable reader.

Results Excellent correlation was demonstrated between data for anti-PGL-I IgM Ab and cytokines obtained with serum and FS blood from the same individuals.

Conclusion The quantitative UCP-LF test strips detecting anti-PGL-I IgM Ab and cytokines for the detection of *M. leprae* infection is compatible with fingerstick blood allowing near-patient testing and immediate appropriate follow-up counselling.

OC 8259 THE VALIDATE NETWORK: EXPLOITING SYNERGIES BETWEEN COMPLEX INTRACELLULAR NEGLECTED PATHOGENS TO EXPEDITE VACCINE R&D FOR TUBERCULOSIS, LEISHMANIASIS, LEPROSY AND MELIOIDOSIS

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Background The VALIDATE 'VAccine deveLopment for complex Intracellular negleteD pAThogEns' Network is a Global Challenges Research Fund (GCRF) Network, funded by the UK MRC and BBSRC and led by the University of Oxford and the London School of Hygiene and Tropical Medicine. It aims to accelerate vaccine development for four intracellular pathogens, *Mycobacterium tuberculosis*, *Leishmania* spp, *Mycobacterium leprae* and *Burkholderia pseudomallei*, by creating a network of scientists from around the world in an interactive community, sharing information, learning from synergies and differences, and forming new collaborations promoting cross-disciplinary, cross-pathogen, and cross-continent research.

Membership Currently VALIDATE has 125 members from 66 institutes in 28 countries, including world leading scientists, post-doctoral researchers, postgraduate students, and interested lay members from academia, governmental agencies, industry, and non-profits.

Activities VALIDATE has four activity streams: 1) providing funding to its members, including pump-priming grants for excellent research, training grants for early career researchers, and fellowships to transition post-doctoral researchers to independence, 2) a members' data-sharing portal, to encourage real-time sharing of data, catalysing the application of insights from one field into another, with an in-house Research Data Analyst working on cross-pathogen applications, 3) providing CPD opportunities for our members, including workshops, seminars and a mentoring scheme, and 4) speeding the dissemination of useful and relevant information via a hub website (www.validate-network.org) and social media (@NetworkValidate) where our members can easily find information about new research, relevant funding calls, events, and training, mentoring and other opportunities. Interested parties can read about our funded work, while a searchable directory of members on our website and a free annual meeting facilitates the formation of new collaborations.

VALIDATE is free to join and has an inclusive membership. This network would be of interest to researchers at the EDCTP Forum working on vaccine development for tuberculosis, leishmaniasis, leprosy and melioidosis.

OC 8277 IDENTIFICATION OF NEW CEREBROSPINAL FLUID AND BLOOD-BASED BIOMARKERS FOR THE DIAGNOSIS OF TUBERCULOUS MENINGITIS IN CHILDREN

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Background Tuberculous meningitis (TBM) is the most severe form of extrapulmonary tuberculosis (TB). It mostly affects young children and results in high morbidity and mortality, mainly due to diagnostic delay. There is an urgent need for new tests for the earlier and accurate diagnosis of the disease. We previously identified a 3-marker cerebrospinal fluid (CSF) biosignature (VEGF, IL-13, and LL-37) with potential to diagnose TBM. In the present study, we show that CSF and blood-based biosignatures may be useful in the diagnosis of TBM.

Methods CSF and serum samples were consecutively collected from 47 children that were admitted to the Tygerberg Academic Hospital in Cape Town, South Africa, on suspicion of having TBM. Using a multiplex platform, the concentrations of 69 host markers were evaluated in the CSF and serum samples from all the study participants, followed by statistical analysis to ascertain the usefulness of these biomarkers as diagnostic candidates for TBM disease.

Results Out of the 47 study participants, 23 (48.9%) were finally diagnosed with TBM and 6 (12.8%) were infected with HIV. Several CSF and serum biomarkers showed potential individually as diagnostic candidates for TBM as ascertained by area under the receiver operator characteristics curve (AUC). However, the main findings of our study were the identification of a four-marker CSF biosignature which diagnosed TBM with an AUC of 0.97 (95% CI, 0.92–1.00), and a 3-marker serum biosignature which diagnosed TBM with an AUC of 0.84 (95% CI, 0.73–0.96). We also validated a previously identified 3-marker CSF biosignature (VEGF, IL13 and LL37) in the study.

Conclusion CSF and serum biosignatures may be useful in the diagnosis of TBM in children. Our findings require further validation in larger, multi-site studies after which the biosignatures may be incorporated into point-of-care diagnostic tests for TBM.

OC 8360 GLOBAL HEALTH RESEARCH AND ITS ROLE IN IMPROVING HEALTH AND HEALTH EQUITY IN AFRICA

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Background Health research has the potential to generate knowledge that may be used to improve health and health equity. This has led to calls for African governments to dedicate at least 2% of their national budgets to heath research, but such resource allocations have never been achieved. Rather, most of health research in Africa continues to be funded by high-income countries (HICs) and involves collaborative partnerships between researchers in high-income countries and those in Africa. These research partnerships have many benefits, but they also raise ethical issues related to justice and fairness in global health research.