EDCTP

The power of sharing science

10th European Congress on Tropical Medicine and International Health
Antwerp, Belgium
16–20 October 2017

EDCTP session on

Development, validation and implementation of diagnostic tools in resource-limited settings

19 October 2017 | 15:30-17:00 | Gorilla 5

Supported by the EU

Programme book

About EDCTP

EDCTP's mission is to contribute to the reduction of the individual, social and economic burden of poverty-related infectious diseases in sub-Saharan Africa.

We fund collaborative clinical research to accelerate the development of accessible, suitable and affordable medical interventions to identify, prevent or treat these diseases, including neglected infectious diseases. Our approach integrates development of African clinical research capacity.

EDCTP is a partnership between 14 European and 15 African countries. The EDCTP programme is supported under Horizon 2020, the European Union's Framework Programme for Research and Innovation.

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Diagnosis of poverty-related diseases in sub-Saharan Africa is challenging as the population is predominantly rural and the health systems often have limited resources. New diagnostics that are cheap, reliable and can be used at point-of-care in remote settings are needed to ensure rapid and effective treatment of patients. Following development, these tests will need to be deployed in health systems which have limited regulatory oversight, training and surveillance systems. This session showcases research in poverty-related infectious diseases, including some EDCTP-funded projects, to develop, validate and implement diagnostics in resource-limited settings and will discuss barriers to reach significant public health impact. The four presentations (with time for questions) will be followed by a general discussion of ten minutes.

Chairs

Marleen Boelaert, Institute of Tropical Medicine, Antwerp, Belgium
Ole Olesen, Director of North-North Cooperation, EDCTP, The Hague, The Netherlands

Speakers

1. Sarah Gabriël, Department of Veterinary Public Health and Food Safety, Ghent University, Belgium
   Rapid diagnosis of *Taenia solium* taeniasis and (neuro)cysticercosis in resource-poor areas

2. Marleen Boelaert, Institute of Tropical Medicine, Antwerp, Belgium
   Syndromic approach to the diagnosis of Neglected Infectious Diseases

3. Novel Chegou, Stellenbosch University, Stellenbosch, South Africa
   Towards the development of a field-friendly point-of-care screening test for the diagnosis of TB disease in resource constrained settings

4. Malik Coulibaly, Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ)GmbH s/c West African Health Organisation (WAHO), Ouagadougou, Burkina Faso
   Missed opportunities for early access to infant diagnosis of HIV-exposed infants and care of HIV-infected infants in Burkina Faso

Organisers

Michelle Helinski (EDCTP Project Officer)
Ana Lúcia Weinberg (EDCTP North-North Networking Officer)

Biographies

Marleen Boelaert

Marleen Boelaert MD PhD leads the Unit of Epidemiology and Control of Tropical Diseases at the Institute of Tropical Medicine, Antwerp, Belgium. After her medical studies (Louvain), she worked with Médecins Sans Frontières. She joined the institute in 1994 and supports programs for capacity development in DRC and Nepal. Her Ph.D. (1999) regarded the evaluation of diagnostics for visceral leishmaniasis. Her current research concentrates on control of neglected tropical diseases, mainly leishmaniasis and sleeping sickness, in an elimination context. She is in charge of a large implementation research programme supporting the elimination of sleeping sickness in the Democratic Republic of Congo. She is co-coordinator of the Marie Sklodowska Curie Innovative Training Network EUROLEISH (www.euroleish.net).

Novel Chegou

Dr Novel Chegou is currently a Senior Researcher at Stellenbosch University, South Africa. Dr Chegou was trained as a medical laboratory scientist at the University of Buea, in Cameroon. After working briefly as a laboratory scientist, he moved to South Africa where he completed his postgraduate and post-doctoral studies in the field of tuberculosis immunology. Dr Chegou's research work mainly focuses on biomarkers for the diagnosis of tuberculosis disease and monitoring of the response to tuberculosis treatment. He is particularly interested in the development of simple field-friendly point-of-care diagnostic tools for the rapid diagnosis of tuberculosis disease in resource-constrained settings.

Malik Coulibaly

Malik Coulibaly DDS MPH PhD is a medical epidemiologist and technical advisor for the regional programme support for pandemic prevention in the Economic Community of West African States.
He recently worked as an epidemiologist during the re-emergence of the Ebola outbreak of Guinea. Previously, he worked in a project on HIV/AIDS which aimed to improve the diagnosis and treatment of HIV-infected children in West-Africa. The project was led by a consortium (MONOD ANRS 12206) financed by the French National Agency for research on AIDS and viral hepatitis, EDCTP, and the Luxembourg Institute of Health.

Sarah Gabriël

Dr Sarah Gabriël is the head of the Laboratory of Foodborne Parasitic Zoonoses at the Department of Veterinary Public Health and Food Safety, Ghent University, Belgium. She graduated as a veterinarian from Ghent University, after which she lived and worked for eight years in sub-Saharan Africa, primarily conducting research on parasitic infections. Her PhD research covered *Schistosoma* spp. infections. From 2008-2016, she conducted research on helminth zoonoses for the Institute of Tropical Medicine, Antwerp, Belgium. October 2016 she was appointed at Ghent University, where she is involved in education in veterinary public health and food safety, and conducts research on foodborne parasitic zoonoses.

Ole F. Olesen

Dr Ole F. Olesen joined EDCTP in September 2013 as Director of North-North Cooperation. He studied at the universities of Aarhus, Denmark and Cambridge, UK, as well as at Copenhagen Business School. Dr Olesen holds a Masters and PhD degree in Molecular Biology and an HD degree in international economics. Dr Olesen has considerable work experience in conducting and managing large international projects on pharmaceutical product development. He also worked as assistant professor in pharmacology at Copenhagen University. Dr Olesen worked in the pharmaceutical industry for 10 years, initially as an international project manager and later in the position of Global Project Director. Before joining EDCTP, Dr Olesen was Principal Scientific Officer for Global Health at the European Commission's Directorate-General for Research & Innovation, where he was responsible for research in neglected infectious diseases and for vaccine research activities.

Abstracts are in order of presentation.

Rapid diagnosis of *Taenia solium* taeniasis and (neuro) cysticercosis in resource-poor areas

Dorny, P.[1], Gabriël, S.[2] on behalf of the SOLID consortium

[1] Department of Biomedical sciences, Institute of Tropical Medicine, Antwerp, Belgium
[2] Department of Veterinary Public Health, Ghent University, Belgium

Introduction: *Taenia solium* taeniasis/cysticercosis (T/CC) is a neglected zoonotic parasitic disease complex with significant economic and public health impacts. Currently, there are no cheap, easy to apply, sensitive and specific diagnostic tools available for the detection of this parasite. Recently, the EDCTP-funded SOLID project was initiated with partners from Belgium, Tanzania, Zambia, Denmark and Germany to address this gap.

Aim: The aim of SOLID is to contribute to the implementation of a rapid, cheap and simple point-of-care (POC) test for the detection of *T. solium* taeniasis and (neuro)cysticercosis (NCC) in two resource-poor, highly endemic countries in sub-Saharan Africa. The project also aims to improve the *T. solium* disease recognition, diagnostic and clinical case management capacities of these countries as well as their capacity to conduct diagnostic and clinical studies.

Methods: The lateral flow test from CDC Atlanta was chosen as the POC test to be used in this project. This test combines two well-validated recombinant antigens – rT24H (detection of CCAb) and rES33 (detection of T-Ab) in one test kit to allow for the simultaneous diagnosis of NCC and taeniasis with only one drop of serum or whole blood obtained by finger prick. The study will be conducted in Zambia and Tanzania, at the community and primary health facility levels, respectively.

Results: Field studies will be conducted in order to enroll participants/ patients and collect all samples needed to evaluate the POC test. According to predefined criteria, a number of participants/ patients will receive a CT scan for NCC diagnosis. Also, a number of samples will additionally be tested with the specific reference laboratory tests at regional reference laboratories, with subsets tested in Belgium and Denmark for quality control.

Conclusion: This project will field validate this POC test. If successful it would be a major breakthrough in early neurocysticercosis case- and tapeworm carrier detection and management, contributing not only significantly to improved health outcomes but also to reducing the risk of transmission. Furthermore, it will contribute to obtaining more epidemiological information on infection occurrence and transmission dynamics, facilitating calculations of burden of disease calculations and subsequent advocacy.

Syndromic approach to the diagnosis of Neglected Infectious Diseases

[1] Institute of Tropical Medicine, Antwerp, Belgium

Boelaert, M.[1], Verdonck, K.[1], the NIDIAG Consortium

Introduction: In 2010, the European research network NIDIAG on better diagnosis for neglected infectious diseases (NIDs) was launched to carry out collaborative clinical research and product development in order to improve the diagnosis and management of NIDs.

Aim: NIDIAG's overarching goal was to improve diagnosis of NIDs by generating evidence about the spectrum of causal pathogens of selected syndromes in different epidemiologic settings, developing clinical guidance and optimizing specific diagnostic devices.

Methods: Syndrome-specific investigations were set up using a series of prospective clinical studies. Patients with one of three syndromes were recruited at primary care level in NID-endemic areas and a final diagnosis was established. The knowledge on specific pathogens causing the pre-specified syndrome was then used in a second stage to elaborate diagnostic algorithms. In an interaction with product developers several immediate gaps were identified and addressed.

Results: This talk focusses on the clinical research of the NIDIAG consortium and some of the challenges and lessons learned. The harmonisation of diagnostic and clinical procedures in multi-country studies is frequently not sufficiently addressed and, particularly in low- and middle-income countries, training and adherence to GCP/GCLP guidelines are particularly challenging. The contribution of qualitative studies assessing the provider perspective was essential to develop appropriate clinical guidance.

Conclusion: The establishment of a quality assurance system that includes internal and external quality control and monitoring activities was a condition for success. The development of clinical diagnostic guidance for resource-constrained settings should take the provider perspective into account.

Reference(s):

- Boelaert M, NIDIAG Consortium. (2016) Clinical Research on Neglected Tropical Diseases: Challenges and Solutions. *PLoS Negl. Trop. Dis.* 10(11): e0004853. doi:10.137 1/journal.pntd.0004853.
- El-Safi S, Chappuis F, Boelaert M. The Challenges of Conducting Clinical Research on Neglected Tropical Diseases in Remote Endemic Areas in Sudan. *PLoS. Negl. Trop. Dis.* 2016 Nov 3;10(11):e0004736.
- Barbé B, Verdonck K, El-Safi S, Khanal B, Teav S, Lilo Kalo JR, Ravinetto R, Chappuis F, Boelaert M, Jacobs J. Rapid Diagnostic Tests for Neglected Infectious Diseases: Case Study Highlights Need for Customer Awareness and Postmarket surveillance. *PLoS Negl. Trop. Dis.* 2016 Nov 3;10(11):e0004655

Towards the development of a field-friendly point-of-care screening test for the diagnosis of TB disease in resource-constrained settings

Chegou N.N.[1], Jacobs R.[1], Corstjens P.L.A.M.[2], Geluk A.[3], Walzl G.[1], on behalf of the AE-TBC and ScreenTB Consortia

[1] DST/NRF Centre of Excellence for Biomedical Tuberculosis Research and SAMRC Centre for Tuberculosis Research, Department of Biomedical Sciences, Stellenbosch University, Cape Town, South Africa
[2] Department of Molecular Cell Biology
[3] Department of Infectious Diseases, Leiden University Medical Centre, Leiden, The Netherlands

Introduction: There is an urgent need for user-friendly, rapid, inexpensive yet accurate tools for the diagnosis of tuberculosis (TB) disease at point-of-care (POC) in resource-limited settings. We evaluated the utility of host biomarkers detected in serum and plasma samples as tools for the diagnosis of TB disease, in a large multi-centred consortium project, comprising multiple African and European institutions.

Aim: To evaluate the usefulness of host biomarkers detected in serum and plasma samples as diagnostic candidates for TB disease.

Methods: Individuals presenting with symptoms requiring investigation for TB disease were prospectively recruited at primary health care centres situated in six African countries, prior to clinical diagnosis. Using a pre-established diagnostic algorithm comprising of laboratory, clinical and radiological findings, participants were later classified as having TB disease or other respiratory diseases (ORD). Using a multiplex cytokine detection platform, we evaluated the concentrations of multiple host biomarkers in serum and plasma samples, and assessed their diagnostic potential for TB disease.

Results: Out of 716 participants enrolled from five study sites, 214 were diagnosed with TB disease, 487 had ORD whereas six had an uncertain diagnosis. A seven-marker serum biosignature comprising of CRP, transthyretin, IFN-γ, CFH, apolipoprotein-A1, IP-10 and SAA identified on a training sample set (n=491), diagnosed TB disease in the test set (n=210) with sensitivity of 93.8% (95% CI, 84.0-98.0%), specificity of 73.3% (95% CI, 65.2-80.1%), and positive and negative predictive values of 60.6% (95% CI, 50.3-70.1) and 96.4% (95% CI, 90.5-98.8%) respectively, regardless of HIV infection status or study site. In a smaller follow-up study, six-marker plasma biosignatures comprising of relatively new biomarkers in combination with some of the markers in the serum biosignature, diagnosed TB disease with a sensitivity of 100% and specificity of 89.3% irrespective of HIV status. Interestingly, an excellent correlation was observed between biomarkers detected in serum and plasma.

Conclusion: We have identified blood-based biosignatures with strong potential in the diagnosis of TB disease irrespective of HIV infection status or ethnicity in Africa. The development of a field-friendly POC test; adaptable to finger-prick whole blood and based on these biosignatures, is currently ongoing.

Missed opportunities for early access to infant diagnosis of HIV-exposed infants and care of HIV-infected infants in Burkina Faso

Coulibaly, M.[1], Meda, N.[1,2], Yonaba, C.[3], Ouedraogo, S.[4], Thio E.[1], Congo, M.[5], Barry, M.[6], Ye, D.[4], Kam, L.[3], Blanche, S.[7], Van de Perre, P.[8], Leroy, V.[9], for the MONOD Study Group ANRS 12206.

[1] Projet MONOD ANRS 12206, Centre de Recherche Internationale pour la Santé, Site ANRS Burkina, Université de Ouagadougou, Ouagadougou, Burkina Faso
[2] Centre Muraz, Bobo Dioulasso, Burkina Faso
[3] Service de Pédiatrie, CHU Yalgado Ouédraogo, Ouagadougou, Burkina Faso
[4] Service de Pédiatrie Médicale, CHU Charles de Gaulle, Ouagadougou, Burkina Faso
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[7] Groupe hospitalier Necker- Enfants malades, Paris, France
[8] Inserm U1058, Université Montpellier 1, Montpellier, France
[9] Inserm, U1027, Université Toulouse 3, Toulouse, France

Introduction: Universal antiretroviral therapy (ART) is recommended for all HIV-infected children under two years of age since 2010, but early infant diagnosis (EID) is required. We investigated the Prevention of Mother-to-Child HIV Transmission (PMTCT) cascade, the staffing, the quality of infrastructures and the knowledge, attitudes and practices (KAP) of children's caregivers regarding PMTCT, paediatric HIV-infection, EID, and paediatric ART in Ouagadougou, Burkina Faso.

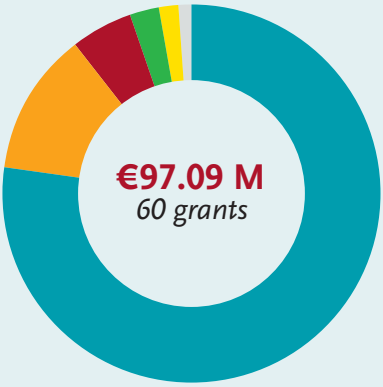
Methods: We conducted a cross-sectional survey in 2011 in all health care facilities involved in PMTCT and paediatric HIV care in Ouagadougou. We assessed their coverage cascade through a desk review of registers and a semi-structured questionnaire administered to health-care workers (HCW). A sociologist conducted a qualitative KAP survey using interviews of caregivers of children <5 years attending paediatric wards.

Results: In 2011, there was no offer of care in primary health care facilities for HIV-infected children in Ouagadougou. Six district hospitals and two university hospitals provided paediatric HIV care. Among the 67,592 pregnant women attending antenatal clinics in 2011, 85.9% were tested for HIV. The prevalence of HIV was 1.8% (95% Confidence Interval: 1.7%–1.9%). Among the 1,064 HIV-infected pregnant women attending antenatal clinics, 41.4% received a PMTCT. Among the HIV-exposed infants, 313 (29.4%) had an EID, and 306 (97.8%) of these infants tested received their result within a four-month period. Among the 40 children initially tested HIV-infected, 33 (82.5%) were referred to a health care facility, 3 (9.0%) were false positive, and 27 (90.0%) were initiated on ART. Although health care facilities were adequately supplied with HIV drugs, they were hindered by operational challenges such as shortage of infrastructures, laboratory reagents, and trained HCW. Out of the 37 caregivers interviewed, 35% stated EID as a strategy. All caregivers thought it was necessary to treat HIV-infected children, although they did not know what interventions could be used.

Conclusions: The PMTCT cascade revealed bottlenecks in PMTCT interventions and HIV EID in Ouagadougou in 2011. The staffing in HIV care and quality of health care infrastructures were also insufficient. Community awareness programs should be strengthened to inform caregivers and improve the uptake of EID and care.

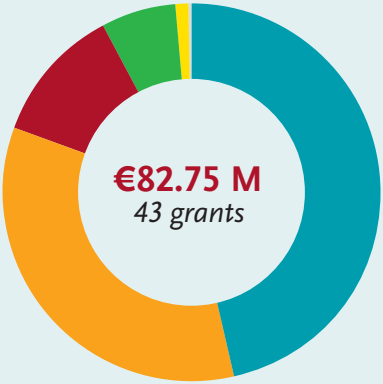
Overview of EDCTP portfolio 2014–2016

By activity



- Clinical research, *13 grants*
  €75.11 M
- Networks of Excellence, *4 grants*
  €11.98 M
- Fellowships, *26 grants*
  €4.88 M
- Translation of research results into policy, *5 grants*
  €2.43 M
- Ethics capacity and regulatory framework, *6 grants*
  €1.75 M
- Health system preparedness, *6 grants*
  €0.94 M

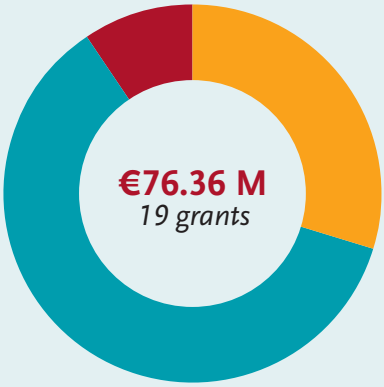
By disease



- HIV & HIV-associated infections, *14 grants*
  €38.58 M
- Tuberculosis, *11 grants*
  €28.28 M
- Malaria, *6 grants*
  €9.46 M
- Neglected infectious diseases, *5 grants*
  €5.34 M
- Emerging diseases, *6 grants*
  €0.94 M
- Diarrhoeal diseases and lower respiratory tract infections, *1 grant*
  €0.15 M

Note: *A further €14.34 million for 17 grants was awarded for projects on non-disease-specific topics such as ethics and regulatory support, networking and fellowship grants.*

By medical intervention



- Drugs (treatment and prevention), *7 grants*
  €46.45 M
- Diagnostics, *11 grants*
  €22.82 M
- Vaccines, *1 grant*
  €7.09 M

Note: *A further €20.73 million for 41 grants was awarded to cross-cutting research activities, ethics and regulatory support, networking and fellowships not related to a particular medical intervention.*

The EDCTP 2017 Calls for Proposals represent a value of 156.5 million euro, 30 million of which will be invested in research on neglected infectious diseases.

Colophon

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The power of sharing science