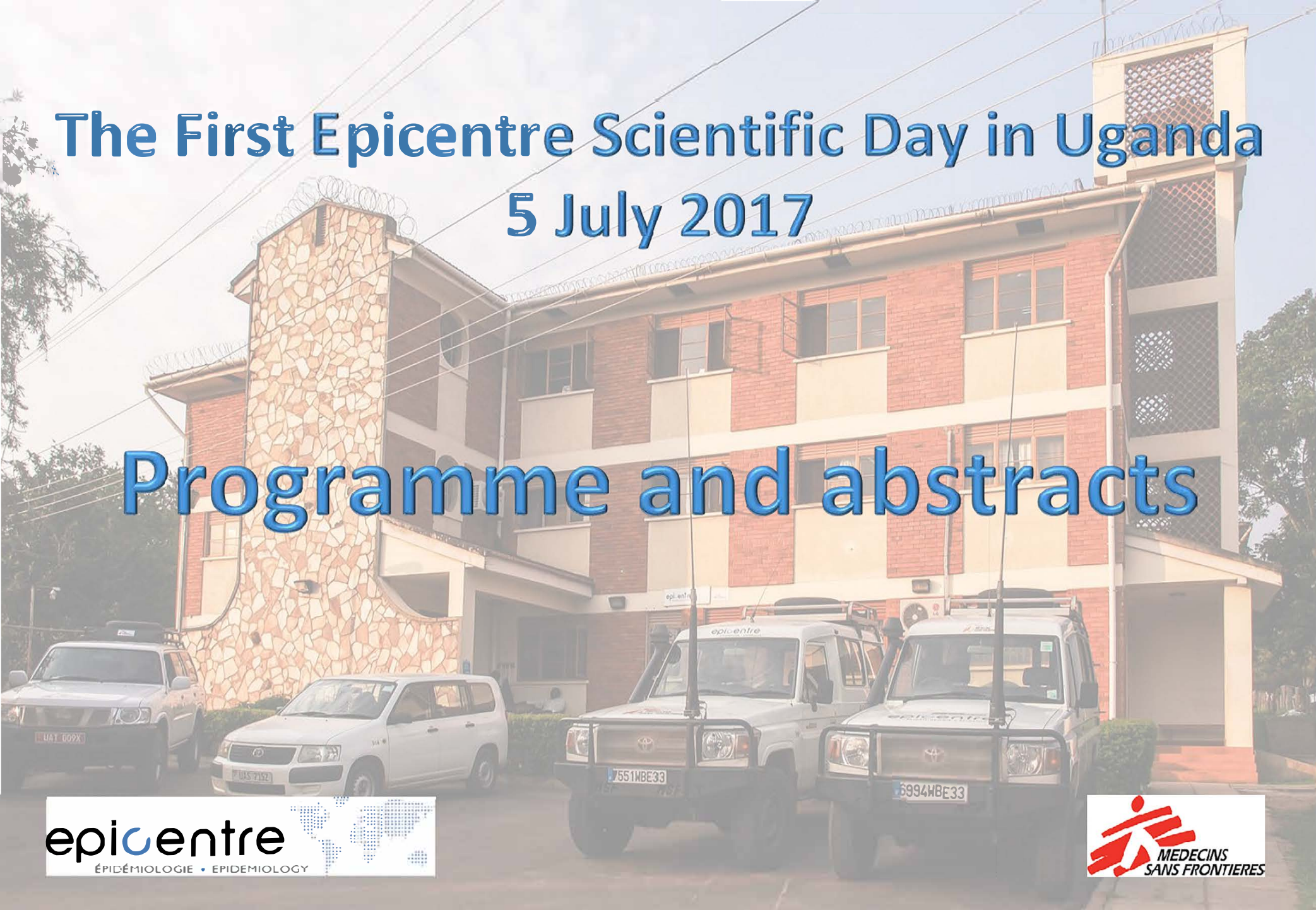
The First Epicentre Scientific Day in Uganda

5 July 2017

Programme and abstracts



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ÉPIDÉMIOLOGIE • EPIDEMIOLOGY

MEDECINS SANS FRONTIERES

Foreword

Welcome to you all!

It is great to see you at the very first Scientific Day Epicentre is organizing in Africa.

Epicentre has provided epidemiological expertise to Médecins sans frontières (MSF) from its Paris headquarters in France for 30 years and has had a base in Uganda for more than 20 years and in Niger for almost a decade. Epicentre Uganda is located at the heart of Mbarara University of Science and Technology (MUST) and Mbarara Regional Reference Hospital (MRRH). At this moment we take the opportunity to thank the University leadership and the ministry of Health that allowed Epicentre to set up a permanent home on its campus from where great work through collaborative effort has been carried out.

Epicentre conducts research and training in support of MSF's goal of providing medical care in areas where people are affected by conflicts, epidemics, disasters, or are otherwise excluded from health care. In these contexts medical doctors do not always have tools to respond adequately to the health needs of the people. Innovation to adapt treatment, diagnostic tools, preventive measures and strategies are needed. These innovations have to be built on evidence without which no policy advance can take place. This is why Epicentre was created and what it continues to do to this day.

Today we have gathered here as people from different walks of life including politicians, diplomats, academicians, service providers, etc., but for one common reason; to forge a way for better delivery of health services. As Epicentre, we are proud to share with you research results that we hope will act as a catalyst to stimulate your thinking further on how to continuously improve health policies and hope to explore with you future research perspectives for Africa.

In the first session we explore research projects that investigate how HIV care strategies can be adapted and improved. This will be followed by a series on how tuberculosis treatment can be safely simplified whilst preserving efficacy. The third session will focus on complex emergencies where epidemiological data need to be made available rapidly in order to mount an effective response. Our last session highlights patients whose needs are neglected despite great suffering. We hope that this last session will stimulate a discussion on health research topics for Africa today.

At the end of the day we will gather for a drink reception where we can continue to discuss today's topics informally.

I hope you have an excellent day!

Dr Juliet Mwanga, Director Epicentre Uganda

Programme
Serena Hotel. 5th July, 2017

8:00 - 9:00 **Registration**

Morning programme

9:30 – 10:00 **Opening Ceremony**

Juliet Mwanga-Amumpaire, Director Epicentre Mbarara Research Centre

Professor Celestino Obua, Vice-chancellor Mbarara University of Science and Technology

Dr Jane Aceng, Minister of Health Uganda

10:00 – 11:00 **HIV/AIDS: Research into adapted strategies to improve access to HIV care**

Moderator: Dr. Joshua Musinguzi, Program Manager Aids Control Program, Ministry of Health, Uganda

- Understanding virological failure in HIV positive adolescents: is it true treatment failure or poor adherence?
  Birgit Schramm
- Fishermen and Fishing communities in East Africa: Most-at-Risk population of acquiring HIV infection. Results from a population-based survey
  Juan Burgos Soto
- Contribution of HIV Population Impact Studies to care strategies : experience of 6 MSF African projects
  David Maman
- *Ongoing project:* Lopinavir-based ART for HIVInfected childreNGlobally (LIVING study)
  Julian Adong

11:00 – 11:30 **Coffee break**

11:30 – 12:30 **Tuberculosis: Optimizing treatment to improve patient outcomes**

Moderator: Dr. Frank Mugabe; Program manager NTLP, Ministry of Health, Uganda

- Rifatox: Is it safe to double the dose of rifampicin to shorten tuberculosis treatment duration?
  Daniel Atwine
- Rifavirenz: Can high-dose rifampicin be an option to shorten tuberculosis treatment for tuberculosis and HIV co-infected patients?
  Maryline Bonnet
- Kids cohort: Pitfalls of childhood tuberculosis diagnosis in high-burden and limited-resource countries.
  Elias KumbaKumba
- *Ongoing project:* TB Speed: Improvement of childhood tuberculosis diagnosis using new technologies for use in low-level health care facilities.
  Eric Wobudeya

12:30-14:00 **Lunch**

Afternoon programme

14:00 – 15:00 **Emergencies and displaced people: research to guide adapted and timely responses**

Moderator: Jean-Luc Anglade, Head of Mission Uganda, MSF France

- Nigeria: Borno crisis, mortality and malnutrition in areas of MSF intervention
  Sophie Masson
- Pneumococcal carriage pre- and post-PCV vaccination campaign in Adjumani refugee camp, Uganda
  Dan Nyehangane
- Dihydroartemisinin piperaquine as intermittent preventive treatment for children in refugee camp
  Matthew Coldiron
- *Ongoing project:* Health assessment and surveillance in refugee camps in Northern Uganda
  Denis Ardiet

15: 00 – 15:30 **Tea break**

15:30 – 17:00 **Research off the beaten track: neglected research topics for neglected patients. Perspectives for future research.**

Moderator: Philip Guerin, Professor of Epidemiology and Global Health, Oxford University

- Oral cholera vaccines: transforming old products in new solutions for neglected populations
  Francisco Luquero
- PSYCa: Developing a tool to identify young children with mental health problems Fabienne Nackers
- Efficacy and safety of a new heat stable rotavirus vaccine (ROSE)
  Amadou Matar Seck
- Antivenoms for snake bites: Combatting market failure and neglect with research
  Matthew Coldiron
- Infection control in the era of antibiotic resistance
  Céline Langendorf

17: 00 – 17:30 **Closure session**

Emmanuel Baron, Director Epicentre, introduces:
Dr. Elioda Tumwesigye: Minister of Science, Technology and Innovation

Juliet Mwanga-Amumpaire closes meeting

17:30 **Drinks**

Session 1

HIV/AIDS: Research into adapted strategies to improve access to HIV care

Understanding virological failure in adolescents living with HIV: Evidence from a cross-sectional assessment and a qualitative study

Birgit Schramm, Epicentre, France

Background

The number of adolescents living with HIV is rising in sub-Saharan Africa, with this patient group experiencing poor treatment and health outcomes. We assessed virological failure and drug resistance to first-line antiretroviral therapy (ART), and qualitatively explored issues influencing adherence amongst adolescents living with HIV (ALHIV) in Chiradzulu, Malawi.

Methods

A mixed-methods study was conducted between May-November 2016.

Quantitative: A cross-sectional assessment included 10-19 year olds receiving first-line ART for ≥6 months. Plasma viral load (VL) was assessed and drug resistance-genotyping performed if VL ≥500 copies/ml. Participants with VL >1 000 copies/ml received counselling and a second VL test.

Qualitative: We explored individual and social influences on ART adherence through in-depth interviews with 16 adolescents, 16 caregivers, seven community members, six health workers, and eight group discussions with ALHIV and HIV-negative adolescents.

Results

Quantitative: 409 adolescents (median age 13 years, 58% female) participated after a median of 6.7 years (IQR: 3, 15) on ART (85% AZT-3TC-NVP, 11% TDF-3TC-EFV). Thirty-two-percent of participants had VL ≥1 000 copies/ml; only 16% supressed to <1 000 copies/ml after counselling. Resistance testing revealed 80% of virological failures were on ≤1 effective drug. Major resistance included 3TC (86%), NVP (93%) and EFV (75%).

Qualitative: Most adolescents reported difficulties adhering to ART despite understanding the importance for their health. Adherence was undermined by individual factors such as poor mental health and inadequate HIV status disclosure, family factors including precarious caretaking arrangements, community factors including stigma; and health services factors such as poor patient-provider relations and overly strict treatment-taking instructions

Conclusions

Treatment failure and drug resistance were high amongst ALHIV in Chiradzulu. A robust once-per-day first-line regimen and frequent VL monitoring should be considered to support adherence and minimize accumulation of resistance. Family-centred approaches are needed alongside youth-friendly health services with tailored counselling and peer-support clubs to help adolescents thrive on ART.

Treatment failure is high among HIV-positive adolescents in Chiradzulu. Multiple social challenges undermine treatment adherence requiring tailored models of care involving families, peers and communities.

Fishermen and Fishing communities in East Africa: Most-at-Risk population of acquiring HIV infection; Results from a population-based survey

Juan Burgos-Soto, Epicentre, France

Background

In East-Africa, fishing communities are considered HIV most-at-risk population but knowledge about the epidemic in these contexts is scarce. Objective: To estimate the HIV-prevalence rate among adults and children in 12 fishing communities surrounding Lake George and Edward, Uganda; and to assess the HIV cascade of care in these settings.

Methods

We conducted a household-based survey. Trained-nurses visited 890 randomly-selected households interviewing adults of 15-69 years old. Blood samples of HIV-positives were collected for viral load measures. Children <15 years old were eligible for testing only if parents were HIV-positive. Logistic regression models, adjusted on socio-demographic behavioral variables were used to identify factors associated with HIV testing and being HIV-positive, and factors associated with HIV-status unawareness and viral suppression among HIV-positive adults.

Results

Overall, 1 738 adults and 148 children were included. The HIV-prevalence rate among adults was 17.5% (95%CI: 15.8-19.4) and among HIV-exposed children 6.1% (95%CI: 3.1-11.4). HIV-prevalence rate was higher among women (20.9%;95%CI: 18.4-23.5) than among men (13.5%; 95%CI: 11.3-16.1). According to occupation and sex, farmers had the highest HIV-prevalence rate among women (27.6%) and fishermen among men (18.7%). After adjustment, only fishermen remained with a 4-fold higher risk of being HIV-positive (aOR: 3.9; 95%CI: 1.6-9.4), compared to men of other occupations. Among HIV-negatives, 81.0% declared having had a test in the preceding 12 months. Among HIV-positives, 86.0% declared HIV-status awareness, 78.0% were on ART and 56.0% virally suppressed. Men had a higher risk of being untested than women (aOR: 2.2; 95%CI: 1.4-3.7) and being virally detectable (aOR: 6.6; 95%CI: 1.9-22.0).

Conclusions

HIV-prevalence rate in Ugandan fishing communities is high, particularly among women and fishermen. Although HIV testing and ART initiation rates are high, viral suppression rate remains poor, especially among men. Nevertheless, fishermen do not seem to have a lower access to care than other men. More HIV preventive interventions are needed in these settings, particularly targeting women and fishermen. Strengthening ART-retention, particularly among men, should be a priority in these settings.

HIV-prevalence rate in Ugandan fishing communities is high, particularly among women and fishermen. More HIV preventive interventions are needed as well as strengthening ART-retention, particularly among men

HIV impact in population surveys in Eastern and Southern Africa

David Maman, Epicentre, South Africa

Introduction

To achieve HIV treatment goals, data are needed on the impact of programs. Epicentre has conducted 6 district based population surveys in 5 countries to measure coverage and impact in HIV programs supported by MSF. The results measured progress toward 90-90-90 goals and guided priorities.

Method

A total of six cross-sectional population surveys were implemented in Ndhiwa (Kenya, 2012), Chiradzulu and Nsanje (Malawi, 2013 and 2016, respectively), Eshowe (South Africa, 2013), Gutu (Zimbabwe, 2016), and Kasese (Uganda, 2016). Using multistage cluster sampling, we recruited individuals aged ≥15 years living in 2 400 selected households in Gutu and 2 443 households in Nsanje, and individuals aged 15-69 years living in 828 households in Kasese. Individuals who agreed to participate were interviewed and tested for HIV at home. All participants who tested positive had their viral load measured, regardless of their ART status. In some studies, we also evaluated CD4 counts, HIV incidence as well as transmitted and acquired resistance.

Results

Among 34 386 adults eligible from 15 473 included households, 30 245 (88.0%) were included and tested for HIV+, ranging from 1 738 in Kasese (inclusion 95.9%) to 7 269 in Chiradzulu (inclusion 87.8%).

The overall HIV prevalence ranged from 12.1% (95%CI 11.2-13.0) in Nsanje to 25.2% (95%CI 23.6-26.9) in Eshowe. In each site, the prevalence was higher among men compared to women ($p<0.01$).

Overall progress toward the 90-90-90 target was: 59/67/83 in Ndhiwa, 77/84/91 in Chiradzulu, 86/94/86 in Gutu, 77/91/89 in Nsanje, and 86/89/68 in Kasese. Each study highlighted that men and HIV-positive individuals younger than 30 were less likely to be diagnosed compared to respectively women or older individuals ($p<0.01$).

Conclusion

These six surveys, with the exception of the first one conducted in Ndhiwa in 2012, showed overall high coverage and highlighted remaining gaps in the cascade of care. In all sites, coverage outcomes were better among women than men, and among older than younger adults, mostly because they were less likely to be diagnosed. Interventions in these settings should emphasize detection of undiagnosed men and young adults.

We performed population-based surveys in 6 sites in 5 African countries to evaluate the coverage and impact of HIV programs. In these settings, we showed that high levels of coverage are achieved. However, detection of undiagnosed men and young adults needs to be reinforced.

Ongoing project: Lopinavir-based ART for HIV-Infected childreNGlobally (LIVING study)

Julian Adong, Mbarara University of Science and Technology, Uganda

Introduction

The revised WHO treatment guidelines reemphasizes the need to treat all HIV-infected children below 5 years of age and, and initiate therapy with a Protease Inhibitor (PI)-based regimen for children less than 3 years of age regardless of prior exposure to antiretroviral in prevention of mother to child transmission (PMTCT) programme . Few antiretroviral drugs are approved for infants and toddlers and existing combination antiretroviral therapies (cARTs) which typically combine Non-Nucleoside reverse transcriptase inhibitors (NNRTI) Nevirapine (NVP) and Nucleoside reverse transcriptase (NRTI) lamivudine (3TC) plus either Abacavir (ABC) or Zidovudine (AZT). They are not optimal for newly infected infants due to their high viral loads (10 to 100 times higher than older children); in addition they are often infected with viruses already resistant to NVP, commonly used for PMTCT. For infants the only alternative to NVP is the PI, Lopinavir, boosted with ritonavir; however the available LPV/r liquid formulations for children taste very bitter, are difficult to administer, and are unstable in tropical climates. This study is evaluating the effectiveness, safety and acceptability of LPV/r pellets in addition to AZT/3TC (or ABC/3TC) paediatric fixed dose combination tablet under routine treatment conditions in HIV infected infants and young children who cannot swallow tablets.

Methods

It is single arm, open-label, prospective, multicenter, multi-country phase IIIb study among children with a past or current documentation of a confirmed diagnosis of HIV-1 infection, eligible for treatment with LPV-based treatment, weighing ≥3 and <25 kg at the time of enrolment and unable to swallow tablets. The primary endpoint is treatment effectiveness at 48 weeks based on a composite endpoint of virologic response <1 000 copies/ml, being alive and on study drug. Patients are followed-up for 24 months.

Status of study

At the Epicentre site recruitment of participants started on 10th May 2016 and so far 68 patients have been enrolled to date.

Existing combination antiretroviral therapies for children are complex, and not optimal for newly infected infants with very high viral loads. There is need to study Lopinavir boosted with ritonavir in pellet form as the available paediatric liquid formulations have a very bitter taste and are unstable in tropical climates.

Session 2

Tuberculosis: Optimizing treatment to improve patient outcomes

Is it safe to double the dose of rifampicin to shorten tuberculosis treatment duration?

Daniel Atwine Epicentre Uganda

Background

The current 6-month TB treatment regimen is still too long. Use of higher doses of rifampicin(R) might ensure faster lung sterilization with subsequent reduction in treatment duration. However, R can induce liver toxicity and safety data using high dose rifampicin are lacking. We assessed whether increasing the dose of rifampicin (R) from 10 mg/kg to 15 or 20 mg/kg, results in an increase in grade 3 or 4 hepatic adverse events and/or serious adverse events (SAE).

Methods

In a Phase IIB, open-label randomized controlled trial in Bolivia, Peru, and Uganda, 300 HIV negative patients with newly diagnosed, smear positive, drug susceptible pulmonary tuberculosis were randomly assigned to one of three regimens containing ethambutol, isoniazid, rifampicin, and pyrazinamide daily for 8 weeks followed by isoniazid and rifampicin daily for 18 weeks. The regimens differed only by the R dose during the first 16 weeks: 1 control regimen with R at 10mg/Kg and 2 study regimens with R at 15mg/Kg (R15) and 20mg/Kg (R20). Serum alanine transferase (ALT) measurements were carried out at regular intervals. Eight week culture conversion was used as surrogate marker for treatment efficacy.

Results

There were 7 grade 3 increases in ALT levels, 1/100 (1.0%) in R10, 2/100 (2.0%) in R15 and 4/100 (4.0%) in R20 regimens respectively (trend test p=0.15). R was discontinued due to liver toxicity in 1 patient (R15). There were no grade 4 ALT increases. There was a non-significant increase in culture conversion rate with increasing rifampicin dosage, 75% (69/92) R10, 82.5% (66/80) R15, and 83.1% (76/91)) R20, (p=0.16).

Conclusions

There was no significant increase in liver toxicity when rifampicin dose increased from 10mg/kg to 15mg/kg or 20mg/kg.

The use of high-dose rifampicin in shortening of TB treatment duration from 6 months to 3 or 4 months can be possible if its safety is assured. Results of RIFATOX trial, show no significant increase in drug-induced Liver toxicity even with doubling of the normal dose of rifampicin.

Can high-dose rifampicin be an option to shorten tuberculosis treatment for tuberculosis and HIV co-infected patients?

Maryline Bonnet, Epicentre, on behalf of IRD UMI 233 TransVIHMI - UM – INSERM U1175, France

Background

Ongoing trials are evaluating high-dose rifampicin (R) regimens to shorten tuberculosis (TB) treatment duration. The risk of drug interaction with some antiretroviral precludes the inclusion of HIV-infected patients. We assessed the effect of high-dose R on the efavirenz (EFV) metabolism in co-infected patients.

Methods

RIFAVIRENZ was a phase-2, randomized, open-label trial conducted in Uganda between 2014 and 2017. Pulmonary TB and antiretroviral therapy (ART)-naïve patients were randomized to 2-study regimens (SR) using high-dose R (20mg/Kg) with ART initiation 2-4 weeks later with 600mg/day (SR_1) or 800mg/day (SR_2) EFV; or to 1-control regimen (CR) using R10mg/Kg and EFV600mg/day. At 8 weeks, all patients were switched to standard R and EFV doses. All patients had intensive pharmacokinetic sampling 4 weeks after EFV-R co-administration, and 4 weeks after R discontinuation. HIV and TB treatment response and safety were monitored.

Preliminary results

Of 97 included patients (SR_1: 31; SR_2: 33; CR: 33), 26.8% were females and median age, weight and CD4 count were 33 years, 53.6 kg and 141 cells/L, respectively. Under R, the median of the EFV minimum concentration (C_{24}) was 1188, 1064 and 1078ng/mL for SR_1 (N=27), SR_2 (N=30) and CR (N=28), respectively. Five (18.5%), 6 (20.0%) and 8 (28.6%) patients had C_{24} < 750ng/mL. At 12 weeks post-ART initiation, 92.6%, 86.2% and 92.6% of patients had HIV viral load < 400 copies/mL. Week 8 TB culture conversion was 88.5% (SR_1), 88.9% (SR_2) and 90.3% (CR). During first 8 weeks, 6 (2 per arm) and 4 patients (SR1: 1; SR2: 2; CR: 1) had transaminase increase ≥ grade 3 and neuropsychiatric events ≥ grade 2, respectively.

Conclusions

Doubling the R dose does not seem to affect the EFV concentrations. These preliminary results need confirmation with the comparison of the EFV pharmacokinetics parameters with and without R.

Trials evaluating high-dose rifampicin short regimens exclude HIV-infected patients due to risk of drug interaction with antiretroviral. Based on the preliminary RIFAVIRENZ trial results, doubling the rifampicin dose does not seem to affect the efavirenz concentrations.

Kids Cohort: Pitfalls of childhood tuberculosis diagnosis in high burden and limited resource settings.

Elias Kumbakumba, Epicentre. Uganda

Background

Diagnosing tuberculosis in children is very challenging, especially in high-burden resource-limited settings. We report the diagnostic findings of a cohort of children with clinical suspicion of tuberculosis at the Mbarara Regional Referral Hospital.

Methods

All children suspected of tuberculosis aged between one month and 14 years received a comprehensive and standardized clinical and biological evaluation including XpertMTB/RIF assay and tuberculosis culture and use of induced sputum in children unable to expectorate. After initial assessment, children with any positive tuberculosis bacteriological test, chest x-ray or clinical presentation that were suggestive of tuberculosis disease were started on treatment. Stools collected from children on treatment were tested with XpertMTB/RIF. At the end of the study, two independent experts reviewed patients' files to classify cases using the 2012 standard case definitions of intra-thoracic tuberculosis.

Results

Of 392 children enrolled, 45.4% were female, 58.1% were younger than 5 years old, 30.1% were HIV-infected and 19.4% had a tuberculosis contact history within the last year. Children < 2 years presented more frequently with severe malnutrition (26.4% vs 5.3%) and were more likely to be diagnosed with a tuberculosis suggestive chest X-ray (50.8% vs 29.2%) compared to children from other age groups. A quarter (25.8%) of the children were tuberculin skin test positive.

Nineteen children (4.8%) were confirmed tuberculosis cases: 18 were either culture or Xpert positive for MTB on respiratory samples and 1 was positive on extra-pulmonary sample. Xpert MTB/RIF on stool had a sensitivity of 57.1% and specificity of 98.2%. Using the standard tuberculosis case definitions, a total of 58/373 (15.4%) children were classified as confirmed or probable tuberculosis. In total, 144 (36.7%) were started on treatment.

Conclusion

This study confirms the difficulties with diagnosing childhood tuberculosis. The majority of cases were diagnosed without confirmation of tuberculosis despite the use of exhaustive diagnostic tests and optimised specimen collection. Rapid, non-sputum based and highly sensitive tests are still needed for diagnosis of childhood tuberculosis. Meanwhile, every opportunity should be taken to improve tuberculosis diagnosis especially among children presenting with severe clinical conditions.

TB Speed: Improvement of childhood tuberculosis diagnosis using new technologies for use in low-level health care facilities.

Eric Wobudeya, MUJHU care ltd & Mulago National Referral hospital, Uganda

Background

Notification of tuberculosis in children is still low. This likely to be due to the paucibacillary nature of childhood tuberculosis, the difficulty to obtain sputum, the low diagnostic yield of existing tests, weak chest radiograph services, lack of systematic screening at all health facility entry points, and absence of point-of-care tests. Improved case detection and access to treatment for children with tuberculosis is a key step to reach the goal of zero death from tuberculosis.

Objective

The TB-SPEED project goal is to contribute to the reduction in childhood mortality from tuberculosis by delivering an available, feasible, cost-effective, and decentralized childhood tuberculosis diagnostic approach to enhance case-finding and access to treatment.

Project implementation plan

This is a four-year UNITAID-funded project implemented in seven countries (Cambodia, Cameroon, Côte d'Ivoire, Mozambique, Sierra Leone, Uganda, and Zambia) to start in September 2017 with three major patient-centred outputs and three technical support outputs building evidence for future scale-up.

The project will innovatively validate a decentralized diagnostic approach using battery-operated GeneXpert OMNI and Xpert ultra cartridge to increase access to tuberculosis diagnostics. It also proposes a simplified nasopharyngeal aspirate sample collection method through the use of battery-operated suction machines that are suitable for rural areas. The project also aims to optimize stool processing without centrifugation allowing stool Xpert testing at lower-level health care facilities. The approach will also include optimized screening, clinical and radiological diagnosis through training, mentorship, the use of digital radiography, and establishment of quality control of X-ray reading.

Project outputs

1. New decentralized childhood tuberculosis diagnostic approaches tested at district health system level
2. Evaluation of an early tuberculosis detection strategy in children with severe pneumonia
3. Validation of diagnostic tools and algorithms in highly vulnerable groups with presumptive tuberculosis, specifically HIV-infected and severely malnourished children
4. Identification of optimized, suitable, and affordable specimen collection and processing methods for childhood tuberculosis diagnosis in resource-limited countries
5. Evaluation of cost-effectiveness of the proposed diagnostic approaches
6. Dissemination, communication and stakeholders' engagement

The TB-SPEED project aims to increase case detection and reduce mortality of children with tuberculosis through decentralization of diagnosis and screening for tuberculosis of children with HIV infection severe malnutrition, or severe pneumonia.

Session 3

Emergencies and displaced people: research to guide adapted and timely responses

Borno crisis, Nigeria. Mortality and nutrition in areas of MSF intervention

Sophie Masson, Epicentre, France

Background

Since 2013, the Boko Haram insurgency and military operations have led to mass population displacement in northeastern Nigeria. From June 2016, MSF was able to operate inside and to lesser extend outside of Maiduguri. We present a series of surveys and surveillance results between July 2016 and May 2017, to describe the health and nutrition status of the population and follow the situation over time.

Methods

In Banki camp, 4 retrospective mortality surveys, using systematic sampling were undertaken between July and December 2016, coupled with malnutrition assessments. In Maiduguri, prospective surveillance of mortality, population size, and malnutrition was carried out in 12 camps in 2016. Retrospective mortality surveys and nutritional assessments were carried out in two unofficial camps between September and October 2016, using exhaustive and systematic sampling. A survey using spatial sampling covering the urban area of Maiduguri–excluding camps–was carried out in November 2016. Cross-sectional population based surveys using spatial cluster sampling were carried out in the catchment areas of MSF nutrition programme to estimate prevalence of malnutrition and programme coverage in May 2017.

Results

In Banki, the initial retrospective mortality and rapid malnutrition screening in July 2016 demonstrated an extremely critical situation. The subsequent surveys showed a rapid decrease of both mortality and malnutrition. The surveys in the two unofficial camps in Maiduguri were also indicative of a critical situation, while the survey of the overall urban areas showed low mortality and malnutrition for both host community and internal displaced people in the community. The surveys in the Maiduguri MSF ambulatory treatment feeding centre's (ATFC) catchment areas showed low prevalence of malnutrition. Nevertheless, admissions to ATFCs remained very high.

Conclusion

The situation in camps assessed outside of Maiduguri were critical, but showed a rapid improvement, despite challenges of accessibility. In Maiduguri, where accessibility to and from the population is less challenging, Overall indicators were much better but there remained pockets of vulnerability". The high number of patients presenting to services is better explained by a large number of people in the area rather than by high prevalence or good coverage.

Following mass displacement of population in Borno state, Nigeria, and subsequent MSF emergency response, various retrospective mortality surveys and rapid nutritional assessments were carried out in order to describe and follow over time the extent of the crisis and its evolution in the areas of MSF intervention. Evaluation of dense urban areas remains a challenge.

Pneumococcal carriage and serotypes distribution pre- and post- PCV vaccination campaign in Adjumani refugee camps, Uganda

Dan Nyehangane, Epicentre, Uganda

Background

In July-September 2014, MSF conducted a mass vaccination campaign (MVC) among children aged between 6 weeks and 23 months in Adjunami settlements using pneumococcal conjugate (PCV-10) vaccines. We aimed to examine the impact of the MVC on pneumococcal carriage and serotypes circulation.

Methods

Three nasopharyngeal (NP) pneumococcal carriage household surveys (respectively in July 2014, March and June 2015) were carried out among residents (all ages). *Streptococcus pneumoniae* was cultured from NP swab specimens. All pneumococcal isolated were serotyped using the Quellung method in Epicentre Mbarara-Uganda Laboratory, in order to describe pneumococcal serotyping distribution in Adjumani population before and after the PCV mass vaccination campaign. In addition, MSF conducted a vaccination coverage cluster survey among children aged between 6 weeks and 23 months in October 2014.

Results

Among children in the age range for vaccination, 96% (95%CI 94-98%) received at least one dose of PCV-10 and 43% (95%CI 39-47%) received 3 doses of PCV-10. Overall pneumococcal carriage increased from 58% (95%CI 56-61%) in the first survey to 67% (95%CI 64-69%) in the third, and from 86% (95%CI 83-90%) to 92% (95%CI 90-94%) among children younger than 24 months. Vaccines serotypes decreased from 37% (95%CI 34 – 40%) to 15% (95%CI 14-18%) overall, and from 49% (95%CI 44-54%) to 17% (95%CI 14-21%) among children less than 24 months.

Conclusion

Following the PCV-10 mass vaccination campaign, NP carriage increased. A significant and rapid replacement of vaccines serotypes by non-vaccines serotypes was observed in all age groups, including non-vaccinated age-groups. Non-vaccines serotypes are expected to be less invasive. Improvement of surveillance of invasive pneumococcal disease is required, together with serotypes circulating in order to monitor the impact of PCV mass vaccination.

Nasopharyngeal pneumococcal carriage increased among the overall population of Adjumani settlements, following a PCV-10 mass vaccination campaign organized between July and September 2014. A significant and rapid replacement of vaccines serotypes by non-vaccine serotypes was observed in all age groups, including non-vaccinated age-groups.

Dihydroartemisinin-piperaquine as intermittent preventive treatment for children in refugee camp

Matthew Coldiron, Epicentre, France

Background

Northern Uganda hosts a large population of refugees from South Sudan, and malaria is one of the major health problems in the area. In 2015, intermittent preventive treatment for malaria (IPTc) was implemented in two refugee camps among children aged six months to 14 years.

Methods

Three distributions of dihydroartemisinin-piperaquine (DP) were conducted at eight-week intervals. The first dose was directly administered at IPTc distribution sites and the second and third doses were given to caregivers to administer at home. A multi-faceted evaluation was implemented, including coverage surveys, malaria prevalence surveys, reinforced surveillance, and pharmacovigilance.

Results

Programme coverage exceeded 90% during all three distributions with a total of 40 611 participants. Compared to same period during the previous year (only available data), the incidence of malaria in the target populations was reduced (IRR 0.73, 95% CI 0.69-0.77 among children under five years old; IRR 0.70, 95% CI 0.67-0.72 among children aged five-14 years). Among those not targeted for intervention, the incidence between the two years increased (IRR 1.49, 95% CI 1.42-1.56). During the intervention, estimates of the prevalence of parasitemia (by microscopy or PCR) ranged between 12.9-16.4%, with the highest prevalence among children aged five-14 years. This increased to 25.3% (95% CI 22.1-28.8) eight weeks after the final distribution. A total of 57 adverse events were reported during the intervention period, including 1 severe adverse event (death from varicella). Adverse events were of mild to moderate severity, and were mainly dermatologic and gastrointestinal.

Conclusion

This is the first documentation of an IPTc programme in a refugee camp. The positive impact of DP on the incidence of malaria, together with its favourable safety profile, should lead to further use of IPTc in similar settings. Expanding coverage groups and decreasing intervals between distributions might provide more benefit, but would need to be balanced with the operational implications of a broader, more frequent distribution schedule.

Preventing malaria in vulnerable populations is a major challenge. The use of DHA-Piperaquine was an effective and safe strategy for intermittent preventive treatment in Uganda

Health assessment and surveillance in refugee camps in Northern Uganda

Denis Ardiet, Epicentre, Paris

Background

Following escalation of violence in South Sudan in July 2016, thousands of refugees crossed the border with Uganda. The Ugandan government settled them into the Bidibidi, and subsequently also the Imvepi settlement. Because they were highly dependent on humanitarian aid, a baseline health and mortality survey assessed their health status. This was followed by the implementation of two different health surveillance systems allowing weekly reporting of most basic health indicators.

Methods

Households were randomly selected by spatial sampling, and household structures were assessed. Nutrition status for children <5 years was evaluated using Mid-Upper Arm Circumference (MUAC) and edema assessment. Retrospective mortality used a 5-months recall period. Two different weekly surveillance systems were implemented, one following the Ugandan community health system and another “lighter” system, focusing on mortality and most epidemic diseases. A second survey was performed for new arrivals to collect more information about mortality in South Sudan and during their journey.

Results

A total of 1 018 heads of household accepted to participate in the baseline survey. The population was found to be very young, and split households were frequent with 20% of that population missing; 32% of households were headed by women. Many households also lacked crucial non-food items. In the settlements, malnutrition and mortality appeared to be below emergency thresholds but delays in food distribution were frequent. On the other hand, crude mortality rates were found to be high in South Sudan with many violent deaths recorded. Surveillance systems revealed small bursts of bloody diarrhea and malnutrition pockets in both settlements.

Conclusions

Our assessments reflected high levels of violence in South Sudan. In the Uganda settlements, health indicators were under control but still need to be monitored.

Health assessment and surveillance among South Sudanese refugees are essential activities, as access to food, water and health services remains fragile.

Session 4

Research off the beaten track: neglected research topics for neglected patients. Perspectives for future research

Oral cholera vaccines: transforming old products into new solutions for neglected populations

Francisco Luquero, Epicentre, Switzerland

Cholera vaccines have only recently become a control tool despite the fact that early prototypes of the currently prequalified cholera vaccines exist since the 1880s. Key research conducted by Médecins Sans Frontières and Epicentre has shown that mass campaigns using oral cholera vaccines (OCV) are feasible in different settings (humanitarian crises, outbreaks and endemic countries), well accepted by the population, and that the vaccines are a safe and effective tool for prevention and response. In addition, we recently demonstrated that short-term vaccine protection can be achieved with a single dose of vaccine, which is a major logistical advantage in response to outbreaks. These key data, along with the creation of a global stockpile managed by the WHO and dedicated funding have led to the doubling of the number of OCV doses delivered worldwide each year since 2012.

However, the significant public health benefit from OCV has not yet been realized because of cost, availability (supply) and logistical constraints. These include a recommendation for two doses, with the second delivered 14 days after the first, high packing volume and cold chain requirements. These factors make vaccine delivery costly and challenging in certain settings. In addition, the complex vaccine formulation translates in suboptimal production, which limits vaccine availability and impedes price reduction (~1.85USD per dose), making the total cost of one fully vaccinated person approximately 6USD.

An improved new generation cholera vaccine could lift these barriers and will bring substantial public health benefits. Any new vaccine should be easier to produce, cheaper, heat-stable and have a reduced storage volume. As one of the main responders to cholera epidemics, MSF could play an important role in pushing for improved vaccines. With better cholera vaccines, used in conjunction with WaSH measures, many more lives could be saved and perhaps the elimination of cholera outbreaks could be foreseen in a near future.

The potential impact of cholera vaccine has not fully materialized because of limitations of current products. New vaccines should be easier to produce, cheaper, heat-stable and with reduced storage volume. MSF and Epicentre could play an important role in pushing for such improved vaccines.

PSYCa: Developing a tool to identify young children with mental health problems

Fabienne Nackers, Epicentre, Belgium

Background

In low-resource settings, the lack of mental health human resources and the absence of cross-culturally validated screening instruments jeopardize the implementation of mental health care, especially for very young children. We aimed to develop and validate a cross-cultural general tool, the PSYCa 6-36, to screen for psychological difficulties in children aged 6 to 36 months.

Methods

A primary validation of the PSYCa 6-36 was conducted in Kenya (n=319 children aged 6 to 36 months; 2014), followed by three secondary validations (n=215, Kenya, 2014; n=189, Cambodia, 2015; n=182, Uganda, 2016). After standardized translation procedures, lay interviewers administrated the PSYCa 6-36 in local languages to the children's caregivers at home. We assessed the psychometric properties of the tool and its external validity against a gold standard (i.e. clinical global impression severity [CGIS] score rated by a psychologist after clinical assessment).

Results

The internal consistency of the PSYCa 6-36 was acceptable (Cronbach's alpha ranged from 0.61 to 0.74) and its temporal reliability was very good (intra-class correlation coefficient [ICC] ≥0.80). The inter-rater reliability was acceptable to good (ICC ranged from 0.60 to 0.83) as well as the external validity (area under the curve ranged from 0.63 to 0.80). The prevalence of CGIS scores ≥1, indicating mental health difficulties according to the psychologist, was 5.1% in Kenya, 8.7% in Cambodia and 10.5% in Uganda.

Conclusion

The results of this study show that the PSYCa 6-36 is a promising screening tool for young children. Once adapted to the local context, the PSYCa 6-36 was easy and quick to use for trained non-specialists. The PSYCa 6-36 also increased the awareness on children's psychological difficulties and the importance of early recognition to prevent long-term consequences. Further use and validation of the tool in settings with higher prevalence of psychological difficulties will help to refine the scale.

The PSYCa 6-36 is a useful tool to screen for psychological difficulties among children aged 6 to 36 months.

Efficacy and safety of a new heat stable rotavirus vaccine (ROSE)

Amadou Matar Seck , Epicentre, Niger

Background

Every year, rotavirus gastroenteritis causes about one-third of deaths due to diarrhea among children under 5 worldwide, most of which occur in sub-Saharan Africa. Infection can be prevented with a vaccine, but a global shortage of the vaccine and the need for cold-chain transport presents delivery challenges.

Methods

We conducted a double-blind, randomized, controlled trial in Niger to evaluate the efficacy and safety of BRV-PV (Serum Institute of India, Pvt Limited), a live, oral, heat-stable rotavirus vaccine. Healthy infants received three doses of vaccine or placebo at 6, 10, and 14 weeks of age. Episodes of gastroenteritis were assessed through active and passive surveillance. The primary endpoint was vaccine efficacy from 28 days post-dose 3. Assuming a 2% attack rate, a 50% true vaccine efficacy, and 20% participant non-assessibility, 117 cases (78 unvaccinated and 39 vaccinated) were required to establish 50% true vaccine efficacy. All serious adverse events, including intussusception, and adverse events were assessed using facility- and home-based surveillance.

Results

Among the 3 508 infants included in the per-protocol efficacy analysis (1 780 in the vaccine group and 1 728 in the placebo group), there were 31 and 87 cases of severe rotavirus gastroenteritis in the vaccine and placebo groups, respectively (2.14 and 6.44 cases per 100 person-years), resulting in a vaccine efficacy of 66.7% (95%CI 49.9–77.9). Similar efficacy was seen in the intention-to-treat analyses. There was no difference in the risk of adverse events (68.7% vaccine and 67.2% placebo) or serious adverse events (8.3% vaccine and 9.1% placebo), including death (n=27 vaccine and n=22 placebo). No child had confirmed intussusception.

Conclusion

We found BRV-PV to protect against severe rotavirus gastroenteritis among infants. BRV-PV does not require refrigeration and represents an important option to prevent morbidity and mortality among the most vulnerable

Rotavirus gastroenteritis leads to about one-third of diarrheal disease deaths in children. We found BRV-PV to protect against severe rotavirus gastroenteritis among infants in Niger

Antivenoms for snake bites: Combatting market failure and neglect with research

Matthew Coldiron, Epicentre, France

Venomous snakes are widely distributed, but most snakebites occur in rural areas of the tropics. Although data are notoriously poor, in Africa, there are an estimated 1 million snakebites, 500 000 envenomings, and up to 30 000 deaths annually.

The venom of any single snake may contain more than 100 different toxins and enzymes, so the clinical result for victims can differ as well. Three major families of toxicities exist: local cytotoxicity (tissue necrosis), neurotoxicity (paralysis), and hematotoxicity (pro-coagulant and anti-coagulant).

Snakebite patients with evidence of envenoming should be promptly treated with antivenom. The choice of antivenom depends on the local epidemiology of snakebites and the availability of antivenoms. If given with minimal delay, antivenoms can drastically reduce mortality associated with snakebite, particularly for hematotoxic envenomings, which typically cause death many hours or days after the snakebite.

Antivenom production is onerous and has changed little since the 19th century. In brief, venom is harvested from snakes and small amounts are injected into a mammal (usually horses). After several months, the equine serum is collected and purified, and anti-venom specific antibodies are collected, and sometimes digested into fragments. Some commercially available antivenoms are species-specific, others are polyvalent.

FAV-Africa (Sanofi Pasteur) is a polyspecific antivenom which covers 10 different species of snakes. It has been the primary antivenom used by MSF across Africa for many years. Its production ended in 2013, and the last doses produced expired in June 2016. Several new antivenoms have entered the market in recent years, but with insufficient data supporting their safety and efficacy. In several settings, MSF is facing challenges over the choice of antivenom (or antivenoms) to use to replace FAV-Africa. Epicentre is conducting studies in the Central African Republic and South Sudan to evaluate and document the use of new products.

Snakebite is a major health problem in rural Africa. Although there are several antivenoms available, there is insufficient data to support their safety and efficacy.

Infection control in the era of antibiotic resistance

Céline Langendorf, Epicentre, France

Prescribing antibiotics without considering the risk of resistance is no longer possible today. First, antibiotic resistance is rising to high levels across the world, threatening ability to treat infectious diseases, even the most common ones. Second, antibiotic resistance is accelerated by the misuse of antibiotics and poor infection prevention and control.

In hospitals and community settings, ongoing research takes a holistic approach by addressing different aspects: diagnosis, treatment and prevention. We are conducting several descriptive studies with the objective of filling in data gaps on the etiologies of bacterial infections, antibiotic resistance and to adapt therapeutic protocols.

The presentation will be based on, first, several etiology studies in children in sub-Saharan Africa; and next on documentation of how antibiotic are prescribed. This provides an insight into gaps and opportunities to improve antibiotic formulation, especially in pediatrics. The use of antibiotic prophylaxis can increase the transmission of multi-drug resistant organisms within the community. Finally, research on infection prevention and control and antibiotic resistance is essential to improve the treatment protocols and reduce the impact and spread of resistance

Antibiotic resistance is rising to high levels across the world, threatening ability to treat infectious diseases. We discuss how research on infection prevention and control and antibiotic resistance can help improve the treatment protocols while reducing the spread of resistance.

Notes

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