



Epicentre Research Base of Mbarara



EPICENTRE

Epicentre is an association created by Médecins Sans Frontières (MSF) in 1987 to help improve the quality of its field interventions. Since 1996, Epicentre has been a World Health Organization (WHO) collaborating centre for research in epidemiology and response to emerging diseases. Epicentre's work hinges around three main activity areas: clinical research, field epidemiology and training.

Clinical research

Epicentre's clinical research focuses on infectious diseases, particularly malaria, HIV/AIDS, tuberculosis, African trypanosomiasis, bacterial meningitis, measles, diarrheal diseases, and hemorrhagic fevers. Epicentre offers expertise primarily in diagnostic and therapeutic clinical trials. Studies are being done in several countries including Uganda, Mozambique, Niger, Liberia, Sudan and the Democratic Republic of Congo. To conduct these studies, Epicentre works in collaboration with research organizations, universities, schools and institutes of tropical medicine. The results from these studies are published in scientific journals and presented at international conferences.

Field epidemiology

Epicentre conducts epidemiological surveys in developing countries, usually in the context of complex emergencies. The surveys are intended to guide interventions in these precarious contexts, and to assess their efficacy. When requested by MSF, other NGOs, or the WHO, Epicentre epidemiologists are brought in to investigate epidemics, conduct field surveys, set up and assess surveillance and alert systems, and assess the impact and coverage of medical programs in areas like infectious diseases, malnutrition, mental health, vaccination, and natural and human-made disasters.

Training

Epicentre designs and conducts training modules in public health and epidemiology. These courses, open to health care personnel at all levels, are offered on a regular basis in Europe and can also be given, upon request, in the field (Africa, Asia, and Central America).

Epicentre in Uganda

In 1995, Epicentre settled permanently in Uganda to regionally support MSF sleeping sickness projects. In Mbarara, in 1997, a shigella resistance study was conducted by Epicentre followed by an antimalarial resistance study (1998/1999). Since then, others studies followed and, over the years, Epicentre conducted a significant amount of research in Mbarara.

The primary role of Epicentre in Mbarara is to conduct high standard clinical research, with important GCP* (Good Clinical Practice) requirements, on critical public health burdens in Uganda and Africa. To reach this objective, Epicentre collaborates with the Mbarara University of Science and Technology (MUST) and its skilled personnel. A full-time experienced research team is now based at the Epicentre Mbarara Research Base (EMRB).

In the last 10 years, Epicentre has conducted many researches on malaria. The results of those studies provided important scientific evidence for changes in malaria control policy in East Africa. More recently, Epicentre started a research program on tuberculosis in collaboration with the MUST and Mbarara National Referral Hospital. Infectious disease in children is also an important research topic developed in the EMRB.

Departments of Epicentre Mbarara Research Base (EMRB)

Medical department

The medical department includes medical investigators who ensure the proper conduct of the clinical researches in compliance with the protocols and the GCP requirements. They guarantee the quality of care, the quality standard of the information collected and the full respect of the study participants' rights by applying GCP.

A team of nurses provides quality nursing care to the study participants in a good nurse-patients relationship. The nurses ensure that patients' observations and samples are taken and recorded in accordance to the study requirements.

The pharmacy ensures that all drugs are stored in a secure and appropriate environment and available at all time.

* Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects.

Laboratory

The laboratory is made of three sections: main lab, microbiology section and tuberculosis lab.

The main lab contents the microscopy (blood smears for malaria diagnosis), biochemistry, haematology, and new molecular diagnostic tools such as Polymerase Chain Reaction (PCR) used for the detection of malaria infections not detectable by Microscopy and for the genotyping of malaria parasite. The Real-Time PCR has been recently implemented for the rapid detection of virus (HSV, Enterovirus...) and others pathogen agents (*Streptococcus pneumoniae*, *Neisseria meningitidis*...).

The microbiology section is dedicated to the culture and characterization of microorganisms from blood, cerebrospinal fluid (CSF) and others biological fluids, and the evaluation of bacteria drug susceptibility.

The third section has been implemented as a Bio Safety Level 3 laboratory for the detection and diagnosis of tuberculosis from sputum and CSF sample by using microscopy and culture.

All the tests are performed according to procedures conforming the international quality standard (GCLP).

Data management department

We have a dedicated team in charge of the data monitoring and management. They ensure that study information is collected and kept in accordance with the protocols and GCP guidelines ensuring privacy, confidentiality and safety. We have an internal data monitoring system, and we perform double data entry followed by data cleaning to ensure that data recorded in CRFs and captured in our electronic databases is of good quality.

Logistic department

The major role of this department is to support the research activity by organising fleet management and transportation of study participants, tracing and follow up of the study patients, inventory and stock management, local and international supplies/orders management, safety and security of both the staff and study participants plus taking care of day to day staff welfare.

Administrative department

Such as the logistic section, the main purpose of this department is to help and support Epicentre Mbarara Research Centre and more precisely the good running of the studies. In order to respond to this, administration is in charge of answering and supervising all questions related to Human Resources Management.

Our research directions are

- 1) The assessment and adaptation of new diagnostic strategies to limited resources settings;**
- 2) The adaptation of therapeutic strategies to limited resources settings;**
- 3) The surveillance and collection of information on the burden of major diseases in limited resources settings;**

Current studies

- The epidemiology of malaria among children under five in Mbarara district, Uganda.**

This study is a cross-sectional community based survey made of two rounds (one in January 2010 and the second in June 2010). The general objective is to measure the prevalence of infection with *Plasmodium falciparum* in children under five years at two periods of the year (at the moment of lowest and highest transmission based on the seasonal rainfalls) and to compare it with the prevalence estimated in 2004 after the rainy season for the same area. Specific objective are the estimation of the prevalence by urban stratum, the analysis of the geographical distribution of the infection, the description of the parasitological characteristics, the assessment of three RDT, the description and the analysis of the prevention and care seek behaviours related to malaria.

- Evaluation of the efficacy and safety of inhaled Nitric Oxide as adjunctive treatment for cerebral malaria in Children: a randomized open label Phase II Clinical Trial**

Despite very effective antimalarial treatment, there is a residual and unacceptable high mortality rate of malaria, especially amongst young children. Recent progress has been made in understanding the role of NO in severe malaria, indicating that NO supplementation is likely to have a beneficial action in severe malaria mainly through down-regulation of inflammatory cytokines like TNF.

Of the various ways to supplement NO, inhaled NO appears to be the safest since it is very well studied in critically ill patients and does not cause systemic vasodilation. This study is a phase 2 clinical trial that aims at demonstrating the efficacy of iNO when added to antimalarial treatment to treat cerebral malaria. This study will also provide a better understanding of the pathophysiological mechanisms involved in severe malaria.

- “Evaluation of the performance of the nitrate reductase and resazurin microtiter assays for the detection of *M. tuberculosis* complex from sputum sample in a high TB and HIV prevalence setting”**

This study aims to assess the use of colorimetric methods (already in use for drug sensitivity testing) as method to provide culture results faster using MGIT and LJ as gold standard. An evaluation of the use of PNB to differentiate Non TB mycobacterium from TB mycobacterium is also part of the objectives.

- “Diagnostic yield and operational aspects of the “String test” to diagnose tuberculosis in children and adults suspects unable to produce good quality sputum, Mbarara, Uganda”**

Tuberculosis diagnosis is a challenge especially in children or in adult who cannot produce sputum. This study aims to assess the use of the string test as method to collect sputum in such patients. This method is compared with the sputum induction.

- **Etiology of infections of the central nervous system among children, Mbarara, Uganda**

Acute infections of the central nervous system (CNS) pose a real clinical problem due to the diagnostic difficulties and the severity of the illness. The organisms responsible for CNS infections cannot be differentiated with certainty based solely on clinical signs. Early etiologic diagnosis is necessary for the proper treatment of these infections and the appropriate use of antibiotics, antifungal or antimalarial therapeutics. This study aims to describe the causative pathogens and the prevalence of acute CNS infections in children (two months to 12 years old) hospitalized at the Mbarara Regional Referral hospital, Mbarara district, Uganda.

Teaching activities

Epicentre participates to the teaching activity of the faculty of Medicine;

- lecture of Microbiology for the 3rd and 4th year of Bachelor in Medical Laboratory Sciences (BMLS)
- Molecular Biology program for the student of the Master of Medical Microbiology.
- Preparation of the curriculum for the new Master in Medical Laboratory Sciences that will start early 2011.

Students of the 3rd and 4th year of BMLS could do the practical part of the teaching in Epicentre laboratory under the close supervision of the laboratory technician.

Some publications of Epicentre work in Uganda

- Clinical efficacy of chloroquine or sulfadoxine-pyrimethamine in children under five from south-western Uganda with uncomplicated falciparum malaria. Legros D *et al. Trans R Soc Trop Med Hyg* 2002;96(2):199-201.
- Artesunate and sulfadoxine-pyrimethamine combinations for the treatment of uncomplicated Plasmodium falciparum malaria in Uganda: a randomized, double-blind, placebo-controlled trial. Priotto G *et al. Trans R Soc Trop Med Hyg* 2003;97(3):325-30.

- Adherence to a six-dose regimen of artemether-lumefantrine for treatment of uncomplicated Plasmodium falciparum malaria in Uganda. Fogg C, *et al. Am J trop Med Hyg* 2004;71(5):525-30.

- Antimalarial efficacy of sulfadoxine-pyrimethamine, amodiaquine and a combination of chloroquine plus sulfadoxine-pyrimethamine in Bundi Bugyo, western Uganda. Checchi F *et al. Trop Med Int Health* 2004;9(4):445-50.

- Supervised versus unsupervised intake of six-dose artemether-lumefantrine for treatment of acute, uncomplicated Plasmodium falciparum malaria in Mbarara, Uganda: a randomised trial. Piola P *et al. Lancet* 2005; 365(9469):1467-73.

- Supervised versus unsupervised antimalarial treatment with six-dose artemether-lumefantrine: pharmacokinetic and dosage-related findings from a clinical trial in Uganda. Checchi F *et al. Malar J* 2006;5:59.

- Molecular genotyping in a malaria treatment trial in Uganda - unexpected high rate of new infections within 2 weeks after treatment. Mugittu K *et al. Trop Med Int Health* 2007;12(2):219-23.

- Assessment of three new parasite lactate dehydrogenase (pan-pLDH) tests for diagnosis of uncomplicated malaria. Fogg C *et al. Trans R Soc Trop Med Hyg* 2008; 102(1):25-31.

- Dihydroartemisinin-piperaquine and artemether-lumefantrine for treating uncomplicated malaria in African children: a randomised, non-inferiority trial. Bassat Q. *et al. Plos One* 2009; 4(11):e7871.

- Efficacy and safety of artemether-lumefantrine compared with quinine in pregnant women with uncomplicated Plasmodium falciparum malaria: an open-label, randomised, non-inferiority trial. Piola P, Nabasumba C, Turyakira E, *et al. Lancet Infect Dis.* 2010

- Artesunate versus quinine in the treatment of severe falciparum malaria in African children (AQUAMAT): an open-label, randomised trial. Dondorp AM, Fanello CI, Hendriksen IC, *et al. Lancet* 2010; 376:1647-1657.