The age of Africa

In this honest and revealing interview, Professor Agrégé Abdoulaye Djimdé explains his work conducting clinical trials of antimalarial drugs in West Africa, and the progress being made towards extending malarial research on the continent, for the continent

How has your career path – starting and finishing at the University of Bamako, with time spent in the USA – led to your involvement in this clinical trials project? What are your main motivations for carrying out this work?

I trained as a pharmacologist at the University of Bamako, Mali, and as a microbiologist and parasitologist at the University of Maryland, USA. Ever since I was a child I have wanted to contribute to reducing human suffering from malaria. As a pharmacologist, I was naturally driven towards working on drugs. Initially I started investigating the molecular mechanisms of antimalarial drug resistance – a process I am still involved with today. Then, when we lost chloroquine to resistance and had to search for replacement drugs, I started working on the clinical development of the new artemisinin-based combination therapies (ACTs).

Why is it important that African scientists are fundamentally involved in the international effort to control malaria?

Malaria is primarily a problem for endemic countries, including those in sub-Saharan Africa. Intimately involving African scientists in the control, elimination and eradication of malaria is of paramount importance; firstly because it is a problem each of us lives with. The majority of African scientists have either personally suffered from malaria, or have a family member or a relative who has been affected – I personally have lost one brother and several nephews and nieces to malaria. Secondly, the intimate knowledge of the local conditions and communities can only be found in those people that belong to the very communities we are dealing with, which is a critical asset for any successful enterprise in this field.

In addition to your primary objective of testing the efficacy of ACT therapies, what are the secondary objectives of your project?

Our network has a wealth of other objectives including the investigation of ACT safety in our specific context and study design; addressing basic research questions such as the impact of the different combinations on gametocyte infectivity, host immune response, molecular markers of drug resistance, pharmacokinetics, pharmacogenomics, etc. This very large study will provide us with a huge mine of biological samples that can be used many years down the road for various purposes.

What are the main aims of the networking meetings that have been organised? Who were the attendees and what were the key outcomes?

Our networking meetings have had various focuses and reflect the natural development of the consortium. We started by getting to know each other better, then planning the studies and their actual execution on the ground. Our current meetings are focused on what to do with the samples we have been collecting, and future ones will deal with data analysis, sharing and publication issues. Along the way, both the southern and northern collaborators are coming together as a cohesive and unique team with people learning from each other, exploiting the strengths of each collaborator and improving each other in the process.

Do you have any preliminary findings that you would like to highlight?

We recently published one of the first African papers on the in vivo efficacy of artemisinin monotherapy, as measured by parasite clearance time – and many more exciting results are on the horizon.

What are the challenges that must be overcome to carry out clinical trials in West African countries such as Burkina Faso, Guinea and Mali?

Although there are overarching issues, the challenges are basically dependent on the level of development of research in the institutions involved. Challenges include: working with communities where access to healthcare services is very scarce; making the distinction between protocol-specific requirements and general healthcare services – often provided by the same team in the same setting; and limited experience of the ethical and regulatory bodies involved. Furthermore, at a logistical level; ensuring the supply chain for reagents and consumables runs smoothly is another hurdle in countries where biomedical research is in its infancy, and maintenance of laboratory equipment is a major problem encountered when conducting clinical trials in developing countries. Finally, in addition to these problems, when one starts work in an institution new to research, training personnel and engaging effectively with local authorities and communities become two further layers in the myriad of issues to deal with.
Health starts at home

A network of African scientists, including researchers at the University of Science, Techniques and Technology of Bamako, Mali, has been conducting trials of antimalarial drugs for use on their own doorstep.

Martin Luther King Jr famously said that ‘injustice anywhere is a threat to justice everywhere’. In many ways, the same could be said of health problems. We are lucky enough to live in a world where threats like malaria – endemic in certain countries but absent in others – are not considered the sole problem of the people who live in affected areas. Rather, researchers all over the world have united in their recognition of a gross threat to human health, regardless of its geographical remoteness from their own homes. Although controversies over the cost of medicine in developing countries continue to arise, the overall picture is of a global community of scientists working to provide solutions for those most in need of them.

But while this approach may showcase some of the finer aspects of the collaborative human search for knowledge and innovation for the benefit of others, it does have its issues. Modern technology and travel make working with a disease prevalent on the other side of the world much easier than it has been in the past, but there is still no substitute for personal experience. Everyday observations have led, often by chance, to some of science’s greatest advances – but they would not have done so without close proximity between scientists and phenomena in their immediate environment. In terms of treating malaria, therefore, researchers native to endemic areas could be vital in combating the disease.

Building a Framework

The problem is that the areas most affected by malaria are usually in the most poverty-stricken regions of developing countries and therefore access to trained scientists is often scarce. Beyond this, there is a more fundamental problem in that the infrastructure, education systems and regulatory bodies needed to train and make use of scientists are also frequently underdeveloped or not in place. An institution of science is needed within at-risk countries, and it cannot come from nowhere – for the future of malaria research, and investigations towards other infectious diseases prevalent in Africa, it is of fundamental importance to focus more time and effort on furthering the research capacity of the less developed parts of Africa.

Professor Agrégé Abdoulaye Djimdé is Project Coordinator of the West African network for clinical trials of antimalarial drugs (WANECAM), and believes the time for malarial research conducted by Africans, for Africa is now. WANECAM conducts vital research into various artemisinin-based combination therapies (ACTs), which are the World Health Organization’s (WHO’s) chosen approach for treating malaria in endemic areas. In order to achieve this the network brings together scientists from Djimdé’s native Mali, as well as Guinea, Burkina Faso and The Gambia. With support from the European and Developing Countries Clinical Trials Partnership (EDCTP) and the Medicines for Malaria Venture (MMV), WANECAM is making a big difference to research in West Africa – especially in the area of malaria.

Act on Illness

WANECAM’s studies focus on ACTs, which combine various antimalarial drugs with artemisinin, a compound derived from annual wormwood, which has been used as an antimalarial in some parts of Asia for thousands of years. They are a particularly effective form of treatment and, because of the variation possible when combining artemisinin with other drugs it is harder for the malarial parasites to develop a resistance to them. The efficacy can be further increased by developing new combinations, so,

Not only has WANECAM made an important contribution to medical research in Africa, but the network has also made significant progress towards improving scientific infrastructure, training and networking activities in Guinea, Mali and Burkina Faso.

A clinical laboratory set up in Kolle, a rural village in Mali.
as Djimdé points out: “The more ACTs we have, the better it is for malaria patients”.

The WANECAM clinical study compares the incidence of uncomplicated malaria in children and adults treated with repeated ACT over a period of two years. The study makes use of populations in three of the countries covered by the network, and sees ACTs, pyronaridine-artesunate (PA) and dihydroartemisinin-piperaquine (DHA-PQP) each compared with artesunate-amodiaquine (ASAQ) or artemether-lumefantrine (AL). Whereas the majority of clinical trials focus on a single treatment and follow-up analysis, this study reflects real approaches to malaria more closely by following patient progress. In practice, these ACTs would be used repeatedly over several years to treat consecutive cases of malaria in the same patients.

By following patients over an extended period and within a large sample size, WANECAM allows for a more realistic interpretation of how these treatments work and provides an opportunity to catch any rare or infrequent side-effects. As well as comparing the efficacy of the various treatments, the trial also aims to accomplish a number of important secondary objectives, directed towards gathering additional data on the treatments’ effects. The assessment of safety using each of the ACTs in repeated therapy; the search for novel molecular markers of antimalarial drug resistance; the comparison of re-infection and recrudescence rates by polymerase chain reaction (PCR); the comparison of gametocyte infectivity and parasite clearance rates; and the impact of immunity, pharmacokinetics and pharmacogenetics, will all be part of the study.

PROVING POTENTIAL

Not only has WANECAM made an important contribution to medical research in Africa, but the network has also made significant progress towards improving scientific infrastructure, training and networking activities in Guinea, Mali and Burkina Faso. These groundbreaking initiatives have come in many forms, but some of the most impressive steps have been the construction of new clinical research facilities – as well as the renovation and refurbishment of old ones – which in places required the installation of electricity, running water and high-speed internet. The cold chain required for sample storage and transport was also upgraded, or created from scratch where necessary, and these new facilities represent the infrastructure foundation necessary for further, even more ambitious studies into malaria and other infectious diseases.

Physical facilities, however, are only half the battle – something that the researchers at WANECAM understand very well. The development of human capacity for research is integral to growth in this area, which is why the network is training six scientists – three PhD and three Master’s students – in addition to offering short-term training to dozens of young scientists and staff in areas from good clinical and laboratory practice to ethics, finance and even driving. Most dramatically of all, the network has succeeded in enabling Guinea, a country previously lacking any facility for clinical research at all, to contribute more than 800 patients to the clinical trial. In a matter of years, a functional team and facility has been built from scratch – an incredible achievement.

NORTH AND SOUTH

Furthermore, this project has brought the African scientists together with European researchers from Sweden, Germany, France and the UK. “Our northern collaborators bring to the table their vast expertise both in basic research as well as in field research. All of them have worked in various endemic countries and have accumulated important knowledge and know-how” Djimdé explains. In addition to their experience, the European partners also provide access to some of the technologies that even WANECAM has not yet been able to unlock. Collaborations between African countries and between developing and developed countries have been the secret of this project’s incredible achievements, as Djimdé affirms: “Together, we form a true winning team”.

INTELLIGENCE

WANECAM

OBJECTIVES

To understand how the malaria parasite becomes resistant to antimalarial drugs and how that resistance spreads over time and space. This is achieved by conducting field and laboratory-based analyses to explore how the genomes of the malaria parasite, the human host and the mosquito vector interact.

KEY COLLABORATORS

Professor O K Doumbo, USTBB, Bamako, Mali • Dr S B Sirima, CRNFP, Burkina Faso • Professor J B Ouedraogo, IRSS, Bobo Dioulasso, Burkina Faso • Dr A Beavogui, CNFSR Mafenyia, Guinea • Professor A Björkman, Karolinska University, Sweden • Professor C Sutherland, London School of Hygiene and Tropical Medicine, UK • Professor S Borman, Magdeburg University, Germany • Professor S Picot, University of Lyon, France • Dr D Nwakanma, MRC Gambia, The Gambia

FUNDING

The European and Developing Countries Clinical Trials Partnership (EDCTP) • Medicines for Malaria Venture (MMV)

CONTACT

Professor Agrégé Abdoulaye Djimdé
Head of Unit

Molecular Epidemiology and Drug Resistance Unit
Malaria Research and Training Center
Department of Epidemiology of Parasitic Diseases
Faculty of Pharmacy
University of Science, Techniques and Technology of Bamako
PO Box: 1805 Point G
Bamako, Mali (West Africa)

T +223 20 22 81 09
E adjimde@icermali.org

AGRÉGÉ ABDOULAYE DJIMDÉ received a PharmD degree from the University of Bamako, Mali in 1988 and a PhD in Microbiology and Immunology from University of Maryland, USA, in 2001. He is currently Professor of Parasitology and Mycology, Head of the Molecular Epidemiology and Drug Resistance Unit of the Malaria Research and Training Center, University of Science, Techniques and Technologies of Bamako, Mali and Wellcome Trust Sanger Institute’s International Fellow. He has co-authored over 80 scientific publications and sits on numerous Malian, African and International committees on malaria research issues.

NORTH AND SOUTH

Further to the table their vast expertise both in basic research as well as in field research. All of them have worked in various endemic countries and have accumulated important knowledge and know-how” Djimdé explains. In addition to their experience, the European partners also provide access to some of the technologies that even WANECAM has not yet been able to unlock. Collaborations between African countries and between developing and developed countries have been the secret of this project’s incredible achievements, as Djimde affirms: “Together, we form a true winning team”.

WANECAM

West African Network for Clinical Trials of Antimalarial Drugs

CONTACT

Professor Agrégé Abdoulaye Djimdé
Head of Unit

Molecular Epidemiology and Drug Resistance Unit
Malaria Research and Training Center
Department of Epidemiology of Parasitic Diseases
Faculty of Pharmacy
University of Science, Techniques and Technology of Bamako
PO Box: 1805 Point G
Bamako, Mali (West Africa)

T +223 20 22 81 09
E adjimde@icermali.org

AGRÉGÉ ABDOULAYE DJIMDÉ received a PharmD degree from the University of Bamako, Mali in 1988 and a PhD in Microbiology and Immunology from University of Maryland, USA, in 2001. He is currently Professor of Parasitology and Mycology, Head of the Molecular Epidemiology and Drug Resistance Unit of the Malaria Research and Training Center, University of Science, Techniques and Technologies of Bamako, Mali and Wellcome Trust Sanger Institute’s International Fellow. He has co-authored over 80 scientific publications and sits on numerous Malian, African and International committees on malaria research issues.