

Profile Interview: Dr Desiree Witte

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Fanuel Bickton talks to Desiree Witte on her clinical research experience with vaccines in Malawi.



FB: Please, provide us with some information on your background and professional experience.

DW: I was born and raised in The Netherlands. Being the only child in the family, reading was my passion. At an early age I became inspired by a book¹ written by Dr Albert Schweitzer, with stories about his hospital in Lambarene, now Gabon. This marked for me the beginning of a life-time interest in living and working in Africa. With that in mind, I studied Medicine at the University of Amsterdam in The Netherlands and specialized in tropical infectious diseases; subsequently I completed a Masters in Tropical Paediatrics at the Liverpool School of Tropical Medicine.

I gained my first work experience as a medical coordinator with Medecins Sans Frontieres (MSF). During my work with MSF in Lebanon (1987/88), I was confronted with several active cases of vaccine-preventable diseases in children living in the Israeli occupied zone of Southern Lebanon. With the support of the International Red Cross, we acquired permission to enter the restricted area and subsequently were able to organize for the vaccination of all the children in the region, over a period of 3 months.

During my assignment with MSF in Afghanistan (1989/91), I coordinated a measles vaccination campaign during a "cross-border" mission in the Russian occupied province of South Kabul.

In 1992 I finally made it to Africa, where we worked alongside the United Nations High Commissioner for Refugees (UNHCR) to set-up a medical aid program, including vaccinations, for the Mauritanian refugees in Senegal.

My last mission with MSF in Mozambique brought me into contact with Malawi. Travelling over land in Mozambique at that time was very unsafe. The Frelimo/Renamo conflict was at its peak and mines were littered all over the country. Therefore, the safest way of travelling was by plane, a small Cessna operated by "Save the Children", which used Blantyre as its base...the beginning of the Malawi connection!

In the Nineties, many Districts in Malawi were headed by a Dutch District Health Officer (DHO) as part of a bilateral aid program between the Dutch and Malawi Governments. I worked for 2 years in this program, first as a Medical Officer in the Surgical, Obstetrics and Gynaecology and Paediatric Departments of Queen Elizabeth Central Hospital, and subsequently 3 years as a DHO in Mulanje District, which still included Phalombe then. It was a challenging time with HIV emerging, causing havoc and devastation in the work force and straining the hospital resources to the maximum. The Government initiated the co-ordination with Non-Governmental Organisations and the Christian Hospital

Association of Malawi (CHAM), in order to develop and implement an integrated public health care program, based on the Health Delivery Area concept.

As the Public Health services in the District were very much an integral part of the DHO's responsibilities, I still have vivid memories of the 'Wednesday District' visits: setting off at dawn and returning far after dark, with the dedicated members of the District Health Management Team, delivering anything from vaccines, paraffin/gas-bottles for maintenance of the cold chain, salaries, drugs, delivery kits, family planning (then still called child-spacing) materials, chlorine tablets, food stuffs and so on, to the far corners of the District. We would return to the hospital late at night, with cases of obstructive labour and other medical emergencies in the back of the car. The road was bumpy which would often see the obstructive labour cases develop into successful deliveries (under a chitenje, in order to keep the delivery protected from the inquisitive eyes from people in the evening bus coming from Blantyre!).

In 1997 I left Mulanje District to go and pursue a Masters in Liverpool. I undertook my dissertation research ("Micronutrients in breast milk and blood of lactating women") in Thailand.

Asia, in many respects, turned out to be a world of difference compared to Africa and I enjoyed the experience of working there. The enchantment however of the African continent brought me back to Malawi, where I was fortunate to be given the opportunity to start off with two new careers: one as a researcher, and one as a mother of twins!

Following my earlier adventures in implementing vaccine programmes, I developed a long-term research interest in vaccine-preventable diseases. Back in Malawi, I was entrusted to become the country Principal Investigator of three large clinical trials under the auspices of the University of Malawi, College of Medicine and University of Liverpool. In 2002, I conducted a measles vaccine trial, in collaboration with the Centers for Disease Control and Prevention (CDC) Atlanta, the London School of Hygiene & Tropical Medicine (LSHTM) and the World Health Organization (WHO). This study evaluated the serological response to two doses of standard titre measles vaccine in HIV infected and – uninfected infants in Malawi².

In 2007, Malawi participated in the pivoting and exciting Phase III clinical trial of rotavirus vaccine^{6,7} and more recently we completed a Phase II study of the candidate RTS,S vaccine against malaria, an assessment of the safety and immunogenicity of 7 dosing regimens in neonates and infants in Blantyre.

FB: Tell us about rotavirus.

DW: Rotavirus diarrhoea kills almost half a million infants and young children each year³. Over 90% of these deaths occur in developing countries, where access to simple, lifesaving treatment is limited^{4,5}. Rotavirus is found everywhere, regardless of hygienic conditions, and almost all children will have suffered from a rotavirus infection by the time they reach the age of 5 years. Since improvement in sanitation and hygiene will not substantially decrease the incidence of rotavirus disease, the prevention of childhood deaths caused by rotavirus infections will mainly require the use of rotavirus vaccines.

FB: What is the name of the rotavaccine and how was it introduced in Malawi?

DW: Between 2006 and 2009, a Phase III clinical trial of GlaxoSmithKline's human rotavirus vaccine Rotarix™ was conducted in Blantyre, Malawi and in South-Africa^{6,7}. The rationale of the trial was to assess the efficacy, safety and immunogenicity of the vaccine. Despite a high background rate of natural rotavirus infection and a wide diversity of circulating rotavirus strains, Rotarix™ reduced severe rotavirus gastroenteritis episodes by about half. Although the vaccine efficacy is lower in African countries when compared to Europe or the Americas, the vaccine prevents more rotavirus diarrhoea episodes in Africa because of a higher rate of severe disease in this part of the world: the glass of preventing severe episodes of rotavirus diarrhoea might be only half-full, but the ultimate effect depends on how big the glass really is!

Following consideration of the results from the combined Malawi and South-Africa trials, the WHO recommended in June 2009 to include oral rotavirus vaccines in all countries' national childhood immunization programs⁸. This was a tremendous milestone in ensuring that vaccines against the most common cause of lethal diarrhoea reach the children who need them most. The Malawi Ministry of Health applied for GAVI (Global Alliance for Vaccines and Immunization) funding and in 2012 the Rotarix™ vaccine was introduced into the national immunization-program in Malawi, free of charge for all infants in Malawi.

FB: What can you say about the impact of the rotavirus vaccination program in Malawi?

DW: A study on the effectiveness of Rotavirus vaccine in Malawi has found that the risk of diarrhoea and the number of hospital admissions due to severe diarrhoea among infants have reduced by 64 and 43% respectively, since the introduction of the rota-vaccine in 2012⁹. The rotavirus vaccine is found to be highly cost-effective in Malawi and giving the vaccine to children can lower illness costs to families^{10,11}.

FB: What challenges, in general, do you experience in your work as a clinical researcher in Malawi?

DW: Vaccine clinical trials are usually studies recruiting healthy children and taking blood samples is an integral part of the trial. There is no problem with taking a small amount of blood in the context of sick children in hospital but the

acceptability of collecting blood samples from healthy infants in the community is quite a challenge! People in Malawi, like in many other countries in Africa, do not like blood being taken from their children, especially not when it concerns babies and infants. The blood volume needed for antibody testing in these vaccine trials is not much, usually not more than 1ml but the entire procedure, including a needle and the baby crying is not what any mother likes. We need to establish a very good understanding with the mothers, their families and the community, to explain and make them understand why and for what reason we need to take a blood sample from their babies, three or four times over the course of the study. Without the mother's understanding and trust, accusations may arise from the community towards the clinical team of selling the blood, or using it for witchcraft, which may jeopardize the recruitment and retention of children in the trial. Blood in Malawi is always a more delicate issue than we tend to assume.

FB: What other studies are you currently doing or are planning to do?

DW: There are two studies coming up soon. One is the "ABCD Study": AntiBiotic treatment of moderate to severe Childhood Diarrhoea. This study is a WHO-sponsored multi-country randomized double-blinded trial of a 3-day course of azithromycin versus placebo. It is planning to recruit in total 11,500 children in 7 countries: Malawi, Tanzania, Kenya, Mali, Bangladesh, Pakistan and India. Mortality among young children with non-dysenteric diarrhoea in developing countries is high¹². Multi-country evidence shows that bacterial pathogens contribute to childhood diarrhoea and mortality¹². In Malawi, existing VacSurv surveillance^{9,10,11} in the post-rotavirus vaccine era shows a substantial mortality at home among children discharged after having been hospitalised with diarrhoea. Traditionally, according to WHO Integrated Management of Childhood Illness (IMCI) Guidelines, antibiotics were reserved for diarrhoea due to cholera or for dysentery. The hypothesis of the ABCD study is that antibiotic therapy is going to reduce mortality and improve growth even in non-dysenteric diarrhoea.

The second study which is forthcoming is the "RV3" oral rotavirus vaccine study: A Phase II randomised double blind dose-ranging study of the RV3 Rotavirus Vaccine administered as a 3 dose neonate or infant schedule. The sponsor for this trial is the Murdoch Children's Research Institute (MCRI) in Melbourne, Australia. The RV3 rotavirus vaccine has been developed from a naturally occurring strain of rotavirus (RV3) found in healthy babies in an obstetric hospital nursery in Melbourne¹³. The special feature of this strain of Rotavirus is that it did not cause any disease in these babies. The goal of the RV3 Program is to develop an effective, affordable rotavirus vaccine aimed at prevention of rotavirus disease from birth^{14,15}. Administration of the RV3 vaccine at birth may offer earlier protection for infants in developing countries than the currently licensed rotavirus vaccines.

FB: What can you say is your greatest achievement – one that you are most proud of in your life?

DW: It is difficult to pick out one particular thing. There are a few things that I am proud of in both my personal and

professional life...like becoming a mother and being able to see my healthy twin- boys grow and develop into young men, respecting all living things as they do. I am equally proud of my mother who turned 100 years last year! She is still very sharp and every evening, for the last 20 years, calls us from The Netherlands, to keep up to date with our endeavours on this side of the world.

From a professional point of view I think the most exciting thing was taking part in the Rotavirus vaccine study and the subsequent WHO recommendation to include the vaccine in all countries' national childhood immunization programs. It is a privilege and feels good to be able to contribute a small piece to the enhancement of children's lives here.

FB: Any last words?

DW: I have been in Malawi for about 20 years now and it is a real pleasure to be able to live in a country as beautiful and as peaceful as Malawi. I am still working together with the same wonderful team of people I have worked with during the last 3 clinical trials. Malawians make a great team; if you motivate them, they will more than motivate you in return. They are, you know, people that are really having the warm heart of Africa in the right place!

I would like to finish with a quote by Dr Albert Schweitzer: "Success is not the key to happiness. Happiness is the key to success. If you love what you are doing, you will be successful".

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