

Annual Report 2003

Gates Malaria Partnership



The GMP Secretariat is based at the London School of Hygiene & Tropical Medicine



Photo: Anne Koerber

Gates Malaria Partnership

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Abbreviations

ACTs	artemisinin containing combinations	LLN	long lasting net treatments
AFRO	African Regional Office, World Health Organisation	LSHTM	London School of Hygiene & Tropical Medicine
AMANET	African Malaria Network Trust	LSTM	Liverpool School of Tropical Medicine
Bombo	Bombo Hospital, Tanga, Tanzania	MARA/ARMA	mapping malaria at risk in Africa
CBA	Commonwealth Broadcasting Association	MOHP	Ministry of Health and Population, Malawi
CEDHA	Centre for Educational Development in Health Arusha	MRC	Medical Research Council Laboratories, The Gambia
CEEMI	Centre for the Enhancement of Effective Malaria Interventions, Tanzania	MAC	Malaria Alert Centre, Malawi
CHMT	council health management team	MHRA	Medicines and Health Products Regulatory Agency (UK)
CHN	community health nurse	MIM	Multinational Initiative on Malaria
CIAM	Centre for Innovation Against Malaria, The Gambia	MVA	modified vaccinia Ankara
CMP	Centre for Medical Parasitology, University of Copenhagen	NIMR	National Institute for Medical Research, Tanzania
CoM	College of Medicine, Malawi	NMCP	National Malaria Control Programme
CQ	chloroquine	NSGA	Nova Scotia Gambia Association
CSA	chondroitin sulphate A	PAM	pregnancy associated malaria
DANIDA	Danish Agency for Development Assistance	PCR	polymerase chain reaction
DBL	Danish Bilharziasis Laboratory	PHE	peer health education
DFID	Department for International Development	PI(s)	principal investigator(s)
DHMT	district health management team	RCHCS	reproductive and child health care services
DNA	deoxyribonucleic acid	RBM	Roll Back Malaria
EANMAT	East African Network for Monitoring Antimalarial Treatment	RL	repellent lamps
EOC	Expert Oversight Committee	SP	sulfadoxine-pyrimethamine
EPI	expanded programme of immunisation	SPH	School of Public Health, College of Health Sciences, University of Ghana
Gates Foundation	Bill & Melinda Gates Foundation	TAYAM	The Association of Youths Against Malaria
GIS	geographical information systems	TRAP	thrombospondin related adhesion protein
GMC	Ghana Malaria Centre, Ghana	USAID	United States Agency for International Development
GMP	Gates Malaria Partnership	WHO	World Health Organisation
GRTS	Gambia Radio and Television Service	WHOPEP	WHO Pesticide Evaluation Scheme
HIMAL	new systems for prediction and detection of malaria epidemics in the East African Highlands		
IEC	information, education and communication		
IMCI	integrated management of childhood illness		
IPT	intermittent preventive treatment		
IPTi	intermittent preventive treatment for infants		
IRD	L'Institut de Recherche pour le Développement		
ITN	insecticide treated nets		
KCMC	Kilimanjaro Christian Medical Centre		
Lapdap™	chloroproguanil-dapsone		
Lapdap™ PHG	Lapdap™ Public Health Group		

Who are we?

The Gates Malaria Partnership (GMP) is a collaboration between:

- Centre for Medical Parasitology (CMP), University of Copenhagen, Denmark
- College of Medicine (COM), University of Malawi, Malawi
- Danish Bilharziasis Laboratory (DBL), Denmark
- National Institute for Medical Research (NIMR), Tanzania
- Kilimanjaro Christian Medical College (KCMC), Tanzania
- Liverpool School of Tropical Medicine (LSTM), UK
- London School of Hygiene & Tropical Medicine (LSHTM), UK
- Medical Research Council Laboratories (MRC The Gambia), The Gambia
- School of Public Health (SPH), College of Health Sciences, University of Ghana, Ghana
- World Health Organisation, Geneva, Switzerland
- World Health Organisation Africa Regional Office (WHO AFRO), Harare, Zimbabwe

What do we do?

The goal of GMP is to develop a programme of innovative approaches to the control of malaria in endemic countries, particularly those in sub-Saharan Africa by:

- Capacity Development: developing needs-based, sustainable, capacity-strengthening programmes that improve the skills, knowledge and attitudes of those involved in advocacy on the importance of malaria in global health, research, prevention and management of the infection.
- Research: promoting research into new interventions for malaria control.
- Knowledge into Practice: developing mechanisms/systems for transferring malaria related knowledge into use.

Where we work

GMP works in 15 African countries, the UK, Denmark, Pakistan and Bolivia.



Introduction to the Gates Malaria Partnership

The Gates Malaria Partnership (GMP) is a complex research and capacity development programme operating in nineteen countries, fifteen of which are in sub-Saharan Africa. Establishing this programme has proved a challenging task. However, the contributions made by many people are now beginning to reap rewards and good progress has been made during the reporting period July 2002 to June 2003.

Progress

Training centres and research laboratories. Malaria training centres are now established in Ghana, Malawi, Tanzania and The Gambia. Each has embarked upon an innovative capacity development programme. Buildings to house the training centres have been completed in Ghana and Malawi, and work on a new building has started in Tanzania. The new research laboratory at KCMC, Tanzania is nearing completion, and work has begun on a research laboratory at Bombo Hospital, Tanzania.

European Advisors and Capacity Development Co-ordinator. The two European advisors have helped the training centres to develop innovative programmes. The Capacity Development Co-ordinator, Dr Anita Davies, has settled into her post at WHO AFRO in Harare and has started to conduct a skills and knowledge needs assessment for each of the training centres.

GMP postdoctoral fellows. Eight postdoctoral fellows have been appointed; 6 of them are based in Africa (Cameroon, Ghana, Guinea Bissau, Nigeria, Tanzania and The Gambia). All now have projects approved by the GMP Research Committee.

GMP doctoral students. 26 PhD students, 23 of whom come from malaria endemic countries in Africa, commenced their studies in 2001 or 2002. Some interesting results are already beginning to emerge from their work.

Research. Nearly all the \$9 million set aside to support research projects has been committed. All of the major research projects supported fall within the five priority areas set out in the initial proposal to the Gates Foundation. These are:

- Epidemic prediction and the use of geographic information systems in malaria control (2 projects);
- Evaluation of new antimalarials and antimalarial drug combinations (5 projects);
- Evaluation of new vector control methods including insecticides and repellents (3 projects);
- Evaluation of malaria vaccines (3 projects); and
- Management of malaria at the community, household and individual level (4 projects).

Knowledge into practice. Several of the research projects supported through the partnership involve work at the household level. For example, one study focuses on how households make decisions about the choice of malaria control measures and how to pay for them. This will help to bridge the transition between research and practice. In addition, GMP supports the Lapdap™ Public Health Group which is investigating ways in which the new antimalarial Lapdap™ (chloroquine-dapsone) can be used most effectively in Africa. Lessons learned are likely to be relevant to the introduction of other new antimalarials under development. A GMP postdoctoral fellow is Chairman of the East African Network for Monitoring Antimalarial Treatment (EANMAT) which is helping to transfer research findings into health policy in East Africa.

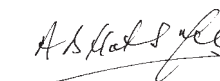
The future

GMP has been an ambitious and innovative undertaking, one of the first of its kind. The process of developing a meaningful, equitable partnership has been a learning process for us all. We must take forward the lessons we have learned from these experiences; so as to ensure the sustainability of GMP.

We hope that you enjoy reading about the many activities in which GMP has been engaged during 2002/03, read on...



Professor Brian Greenwood
Director, Gates Malaria Partnership



Dr Hatib Njie
Chair, Expert Oversight Committee

Capacity Development & Training

The aim of GMP's capacity development and training activities is to develop needs-based, sustainable, capacity strengthening programmes that improve the skills, knowledge and attitudes of those involved in advocacy, research, management and prevention of malaria.

Specific objectives are to:

- Provide multidisciplinary training programmes that use innovative approaches and are responsive to district, country or sub-regional needs;
- Build the capacity and sustainability of the GMP training centres in The Gambia, Ghana, Malawi and Tanzania;
- Provide quality education and training through effective review, monitoring and evaluation procedures; and
- Establish postdoctoral and PhD programmes that strengthen malaria research capability.

GMP Training Committee

The Committee has met four times. The training programmes proposed from each of the centres have been considered in detail and members of the Committee have played an active role in their design and development. The major emphasis of the Committee has been on innovation and quality.

In response to the mid-term internal review of the training programme, the Committee is speeding up the development and approval of proposals and is establishing a working party to monitor and advise on quality assurance and evaluation issues.

PhD students from the countries where GMP centres are based are being encouraged to become involved in the courses run by these centres.

European Advisors

GMP currently has two advisors who assist the training centres in the development and implementation of their training activities, Ms Angela Dawson, an educational advisor, who is based at LSTM and Dr Paul Bloch, a technical advisor who is based at DBL. Two new additional advisors with expertise in quality assurance and educational technology will be recruited to assist in the development of new training materials.

Last year, Ms Dawson worked on a number of innovative media and health education initiatives. Following a successful Malaria and the Media course for forty journalists from four East African nations held in November last year, she has been moderating the electronic discussion list set up to enable these journalists to continue their dialogue. Ms Dawson and CEEMI have been discussing the development of a diploma of health communication with the Tanzania School of Journalism at the University of Dar es Salaam.

In The Gambia, Ms Dawson has been assisting with the development of CIAM's strategic plan and the management of their programmes, working closely with the MRC. She has worked with CIAM, the NGO Tesito, the Commonwealth Broadcasting Association (CBA) and the national broadcaster GRTS to produce a radio soap opera *Bolonghodala*. She has also provided input into the planning and evaluation of the Peer Health Education (PHE) malaria initiative that is soon to be tested in schools across The Gambia, in collaboration with the NGO Nova Scotia Gambia Association (NSGA). She will be supporting the development of a module in participatory malaria programme planning for the Community Health Nurse (CHN) training programme which will be augmented by electronic learning materials. These will draw upon new developments in technology and instructional design.

Ms Dawson is also working on the preparations for the CBA "Health and Broadcasting" African Regional conference in Abuja in September. This conference aims to develop a dialogue between key figures in African broadcasting and those involved in African health research and practice. A workshop during the conference will develop a list of recommendations that will be taken forward to the Commonwealth Heads of Government meeting in Nigeria in December.



Angela Dawson with G.D. Jayalakshmi, the producer of *Bolonghodala*
Photo: Ben Keating

Dr Bloch is actively involved in guiding and supporting the four training centres in Africa, partly through in-service training in relation to strategic planning, protocol and technical skills development and partly by acting as a critical assessor.

The major capacity building programmes in which he is involved include:

- the establishment of drug revolving funds at community level in Mpemba Health Centre catchment area in southern Malawi;
- the strengthening of the health management information system in Mwanza District in Malawi;
- the training of mother and child health workers in the prevention and management of malaria in pregnant women in Muheza District in Tanga Region, Tanzania;
- the strengthening of community-based health services through health systems support and training of health extension workers in Muheza District; and
- the strengthening of community-based healthcare, with an emphasis on mothers and other caregivers' capacity to prevent and handle malaria, in selected districts in rural Ghana.

Capacity Development Co-ordinator

Dr Anita Davies, capacity development co-ordinator, took up her post in February 2003. She is based in the Malaria Unit, WHO Africa Regional Office in Harare, Zimbabwe. This new position links GMP and WHO AFRO roles and activities in taking forward the strategic plan for capacity development for Roll Back Malaria in the Africa Region.

Dr Davies has facilitated a capacity development workshop for malaria consultants organised jointly by the Malaria Consortium and the Malaria Unit, WHO AFRO. She has also been involved in the review of the WHO international course in malaria. She is currently conducting a skills needs assessment of the four training centres.

At the Malaria Alert Centre, College of Medicine, Blantyre, Malawi, Dr Davies facilitated a consultant and focal persons meeting in malaria case management and is working with the Director, Dr Grace Malenga, to determine in-house capacity development needs.



Dr Anita Davies. Photo: LSHTM

GMP Training Centre	GMP Partner	Location
Ghana Malaria Centre (GMC)	School of Public Health, College of Health Sciences, University of Ghana	Accra, Ghana
Malaria Alert Centre (MAC)	College of Medicine	Blantyre, Malawi
Centre for Enhancement of Effective Malaria Interventions (CEEMI)	National Institute for Medical Research	Dar es Salaam, Tanzania
Centre for Innovation Against Malaria (CIAM)	Medical Research Council Laboratories	Fajara, The Gambia

The Training Centres

The long term aim of the four centres in Africa is to be sustainable centres of excellence in malaria training. These centres are now fully operational with a complement of core staff. Following the mid-term internal review, the staff of the centres will be reinforced by recruiting at Director level for three of the centres and by expanding the skills of the existing staff.

For three centres, new buildings are being or have been provided (see the Infrastructure section). The centre in The Gambia is currently operating from rented accommodation.

All four centres have developed their own strategic plans. Whilst different in approach and content they have all been written in consultation with the respective NMCP to meet the needs of their country whilst fulfilling the objectives of the host institution and GMP. These plans will be developed further during the next year, each having a logical framework which will give them a more unified format.

The following sections describe the activities at each centre.



Advocate making a presentation at a training session, Dangme West District. Photo: GMC Team

Ghana Malaria Centre

Most of the year's activities have revolved around the development and implementation of a community-based training programme which focuses on mothers and caregivers. The GMC programme has been piloted in 3 communities in Dangme West District. The pilot process included pre-testing baseline survey tools, training of mother/caregiver advocates, and community-based training by the advocates themselves. The mother/caregiver advocates were selected from identifiable community groups (e.g. seamstresses and dressmakers, hairdressers, farmers associations, traders and opinion leaders). Advocates then trained their group/association members on malaria control issues.

Around 1,900 community members have been trained by the mother advocates. The training programme established a link with the formal health delivery system through the involvement of the district health management team (DHMT) staff as master trainers. The programme also facilitated demand for pre-packaged antimalarial drugs and insecticide treated nets (ITN) with the assistance of KINAPHARMA Ltd and Agrimat Ltd respectively.

A post training survey of the pilot study was carried out and full implementation of this activity has begun in Shama Ahanta and Ashanti Akim North districts covering the period from May to December 2003. The activities include baseline survey, cascade training, monitoring of activities, and post-intervention surveys.

Malaria Alert Centre, Malawi

The centre has been working on five activities during the last year:

- Mwanza DHMT and its community health workers are being trained in community-based data collection and management, building on existing skills that were pioneered in the district for EPI and in the development of a village health register. By monitoring the training and introducing innovative ways of data presentation such as GIS district mapping, MAC aims to improve malaria data management for district health planning and create a model that can be replicated elsewhere in Malawi.
- On-site training of the district health teams in the management of severe malaria in children is being carried out at Ntcheu District Hospital. This activity builds on diagnostic laboratory training which was conducted at the hospital by the Ministry of Health and Population, with support from DFID. MAC is running the management of severe malaria training as a joint effort with the University of Carolina/Centers for Disease Control (CDC). The team has collected baseline data on hospital and community practices in Ntcheu, conducted a needs assessment, and organised on site training visits to the Queen Elizabeth Central Hospital in Blantyre. Areas that could be adapted locally in order to improve severe malaria case management have been explored. In May 2003 MAC hosted a WHO AFRO supported planning meeting for case management of severe malaria in the SADC region. MAC's performance needs assessment process and the critical care pathways monitoring tool being used at Ntcheu were considered to be good innovations.

- MAC is training community health workers and the Mpemba Health Centre management team in the management of drug revolving fund structures in the entire Mpemba health centre catchment area. This is seen as a way of improving antimalarial drug access for the community, and as a public health planning exercise for the health centre staff. Baseline population and malaria morbidity data have been collated on GIS maps and qualitative data on health seeking behaviour are being collected ahead of training.
- MOHP is implementing the national dissemination of laboratory skills training with the objective of improving the management of severe malaria at district hospital level. This is part of the Essential Medical Laboratory Services programme that was pioneered in Ntcheu. MAC is supporting the programme by contributing to evidence based policy implementation.
- A three-week modular training programme for entomology assistants to be deployed for programme and research activities was conducted in June 2003 and included external participants from Tanzania and Zambia. Training modules on vector biology were developed by LSTM and CDC. The need for such training was identified during the RBM needs assessment exercise for Malawi.

Following on a successful course in Tanzania MAC is developing a training proposal for journalists to coincide with a high profile official opening of the new MAC building.

Centre for the Enhancement of Effective Malaria Interventions, Tanzania

A Malaria and Media workshop was held in Tanga, Tanzania in October 2002. It consisted of a one-day meeting involving the Minister for Health and owners/CEOs of media institutions, followed by a five-day workshop for journalists from print and electronic media from Kenya, Malawi, Tanzania and Uganda. The workshop was well received by the participants. An active e-mail discussion group has been set up. Three fellowships were awarded to participants to attend the Multilateral Initiative on Malaria (MIM) Conference in Arusha, Tanzania. More recently, through the influence of CEEMI, four journalists were supported by the NMCP to cover the Malaria & Integrated Management of Childhood Illness (IMCI) conference in Dodoma. Following this workshop, GMP has received requests from African journalists for further workshops (see Malawi Alert Centre).

Continuing the advocacy theme, CEEMI is currently preparing for a one day seminar for all of Tanzania's MPs, to be held in the National Assembly in Dodoma in November; it is hoped that the President of the United Republic of Tanzania will officiate. This will encourage MPs to be more actively involved in malaria campaigns in their constituencies.

Training is planned for community health management team (CHMT) members and healthcare providers in the implementation of intermittent preventive treatment (IPT) in pregnancy in Muheza District. Training of frontline healthcare providers in IPT is seen as a way of strengthening the peripheral level of the formal health system. The activity is designed as cascade training. Three trainers will train ten CHMT members from Muheza who in turn will train two staff from each health centre and dispensary in the district. A change in the proportion of women who take IPT during pregnancy will be an important indicator of success. CEEMI has worked with NMCP, RCHCS, USAID and NIMR to review and update a training manual on "Focused Antenatal Care".



A journalist interviews the head of the Vector Control Training Centre, Tanzania. Photo: Jasper Ijumba

Centre for Innovation Against Malaria, The Gambia

Two activities have been implemented during this year. The first involves the addition of a malaria component to an established school-based, peer health education programme run by the NGO NSGA. The overall goal of NSGA's PHE programme is to improve the health and well-being of youth by empowering them with the knowledge, skills and confidence to take responsibility for their own health. The additional aim of the malaria component being implemented with CIAM is to extend the knowledge skills and attitudes to malaria to mothers of children under five.

The programme started in September 2002 with the training of the regional co-ordinators of NSGA. The impact of the programme is being measured in the pilot phase by assessing malaria knowledge gain among PHEs, schoolchildren and mothers/carers of children under 5 years in selected communities. The second phase is planned for August/September 2003 and will evaluate the intervention using a community-randomised approach.

This second activity involves the development of 26 episodes of a radio soap opera called *Bolonghoda* to be broadcast by Gambia Radio and Television Services (GRTS) from July 2003. The drama is set in a fictional, but typical, rural Gambian village and combines stories about the struggles of ordinary people with messages about malaria prevention. Five radio listening clubs have been set up in Julangel village to give the community a structured forum for discussion of each episode. The episodes are presently being recorded as well as two short films, one an advertisement for the soap opera and the other a CIAM promotional video. CIAM is working in close collaboration with the NGO Tesito, GRTS and the CBA on this project.



CIAM's Field Assistant James with PHE and family, The Gambia.
Photo: Ben Keating

Two further activities are being developed. The first involves training the CHNs to work with communities to develop malaria control programmes. During the development of the proposal, CIAM received support and input from the Director of Health Services, the Principal Tutor of the CHN School, the NMCP, the Chief Nursing Officer and other partners. The project is expected to run to the end of 2005. The second activity under development is the production and filming of a malaria video for the PHE intervention. It will be shown during the second phase of the PHE project starting in September 2003. The non-intervention schools in the second phase of the PHE project will be shown a tuberculosis video; each can then serve as a control for the other when the impact of the programme is evaluated.

Profile of Balla Musa Joof, Assistant Training Co-ordinator, CIAM

Balla was born in Mbollet-Ba, a village in the North Bank Division of The Gambia. In 1992, following a course in public health at Gambia College he joined the Ministry of Health as a Senior Health Superintendent, serving in various health divisions throughout the country. Initially his interest was human nutrition but, in 1997, when working in Bakau, malaria took the life of an 8-year-old girl of a family that he was very close to. From that time on he was determined to make an extra effort in the fight against malaria.

The Association of Youths Against Malaria (TAYAM) was formed in 1997. Its objective is to reach every family in the Bakau area with simple messages on how to prevent and treat malaria. Balla co-ordinated the activities of TAYAM for five years, and the organisation is continuing to make significant efforts on IEC and advocacy for malaria control.

In 1998, Balla received a scholarship to pursue a Master's degree in Public Health at the University of Maastricht in the Netherlands. After completing his studies he accepted a teaching position at Gambia College's School of Public Health. Balla joined CIAM as the Assistant Training Co-ordinator in July 2002. His long desired goal of reaching everyone with simple malaria messages is now becoming a reality.



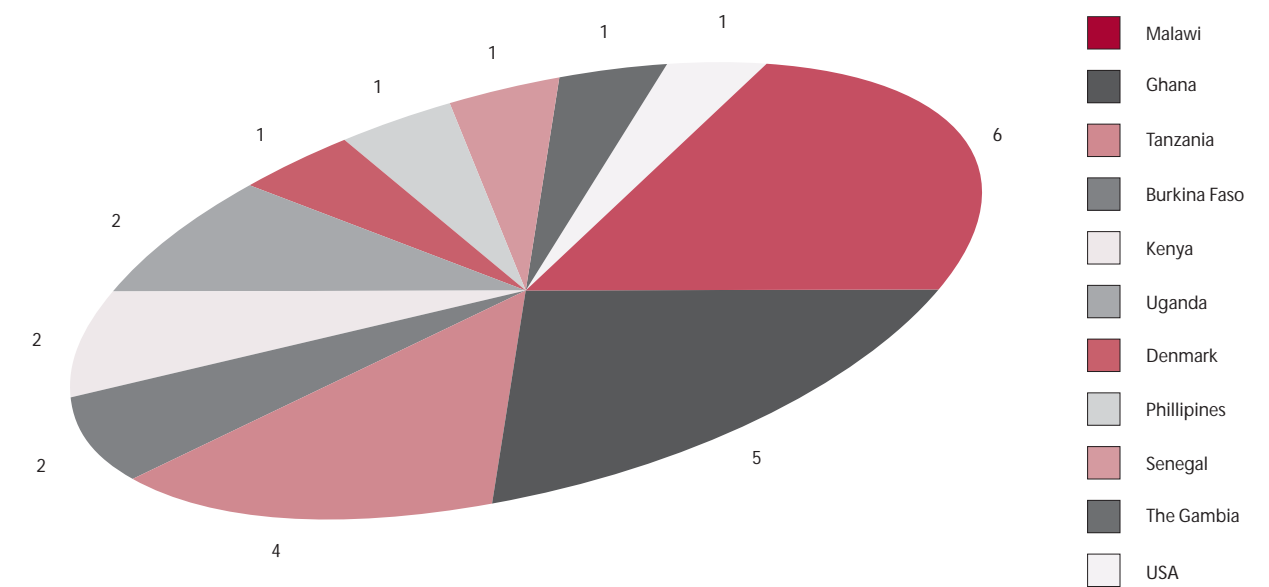
Balla with a traditional communicator. Photo: Ben Keating

He is proud to be part of the team at CIAM, working closely with national and international partners. He feels he is learning a lot of new things through GMP. Balla is engaged, and as the clock ticks, the marriage bells are ringing louder and louder! He likes R & B music and photography and has a great interest in computers.

GMP postdoctoral programme

Eight postdoctoral fellows, six of whom are based in Africa, have been appointed and are in post. All postdoctoral fellows have submitted competitive proposals to the GMP research Committee. The table below shows their approved projects.

GMP postdoctoral fellows and their projects	
GMP postdoctoral fellows	Projects
Dr Kalifa Bojang Clinician MRC The Gambia	Phase IIb studies of heterologous prime-boost immunisation against malaria infection in The Gambia A study of the efficacy of IPT with SP in preventing morbidity in Gambian children treated for severe anaemia
Dr Siân Clarke Epidemiologist LSHTM	The cost effectiveness of malaria prevention in pregnancy in an area of low transmission in Uganda
Dr Wilfred Mbacham Biochemist/Public Health Specialist University of Yaounde, Cameroon	Antimalarial drug resistance and markers of therapeutic efficacy in Cameroon
Dr TK Mutabingwa Clinician Teule Hospital, Muheza, Tanzania	An open-label, randomised, four-arm trial of SP, SP-amodiaquine, artemether-lumifantrine and amodiaquine-artesunate in mild-moderate malaria in Tanzanian children Treating malaria in pregnancy: a randomised trial of potential options for treatment in an area of high drug resistance in Tanzania
Dr Obinna Onwujekwe Clinician/Health Economist University of Nigeria, Enugu, Nigeria	Private and public providers of malaria treatment services in Nigeria: economic, equity and performance analyses
Dr Seth Owusu-Agyei Epidemiologist Kintampo Health Research Centre, Ghana	The pattern of <i>P. falciparum</i> in the Kintampo District in the middle belt of Ghana
Dr Amabélia Rodrigues Epidemiologist Bandim Health Project, Guinea-Bissau	The effect of <i>Bacillus Calmette Guerin</i> vaccine on malaria morbidity and mortality
Ms Virginia Wiseman Health Economist LSHTM	An investigation of the economic and socio-economic determinants of the demand for malaria treatment



GMP doctoral students programme

Twenty-six studentships have been awarded, 23 to students from African malaria endemic countries (see pie chart above). Sixteen come from one of the four countries with a GMP training centre, and most are linked to a centre.

Most students who commenced their studies in 2001 are now fully engaged in their field or laboratory work. Students commencing their studies in 2002 have either started or are finalising their preparations for field or laboratory work. The GMP doctoral students met at Usa River, Tanzania just prior to the 2002 MIM Conference. This was an excellent opportunity for students to share their experiences so far. They will have another opportunity to meet together at the British Society of Parasitology meeting in Chester in May 2004.



The PhD students meet at Usa River, Tanzania. Photo: Cathy Bowler

PhD Sunday

Numerous requests are received by GMP from capable scientists from African malaria endemic countries for PhD funding. An interim proposal for further funding for additional PhD students will be submitted to the Gates Foundation later in 2003.

Profile of a GMP doctoral student: Danish Bilharziasis Laboratory

Dr Sheick Oumar Coulibaly, National Public Health Laboratory, Burkina Faso

Oumar is a medical doctor from Burkina Faso, specialising in clinical biology with a Masters degree in Parasitology. He was an assistant researcher in malaria and parasitic diseases at Centre Muraz until October 2001 when he was promoted to Head of the Clinical Biology Department of the National Public Health Laboratory. In November 2002, he was made an assistant lecturer in parasitology at the Faculty of Medicine of the University of Ouagadougou.

Oumar completed the research methodology course at DBL and then received a GMP PhD studentship in 2001 to complete his PhD under the supervision of Prof Thor Theander and Dr Pascal Magnussen. His project, which started in October 2002, involves investigating the relationship between the use of antimalarial drugs in pregnancy and *Plasmodium falciparum* resistance.



Sheick Oumar Coulibaly. Photo: SOC

Profile of a GMP doctoral student: Centre for Medical Parasitology

Mr Ali Salanti

Ali Salanti was born in 1974 in Denmark. When he left school he spent two years backpacking in Africa, Asia and South America. He then completed a first degree in biology at Copenhagen University. During this time he worked on a Village Concept Project in Zimbabwe; this led to his interest in malaria research. He specialised in molecular parasitology and started working for the Centre for Medical Parasitology in 2000. In 2001 Ali obtained a MSc in biology. The same year he started a PhD programme funded by GMP.

His project is on the identification and characterisation of a vaccine candidate against pregnancy-associated malaria (PAM). The malaria parasite, *P. falciparum* binds to capillaries to avoid being filtered through the spleen where they are killed.

This binding is mediated by a group of variant proteins called PfEMP1. Antibodies against PfEMP1, which prevent binding, are important for acquisition of immunity. In women suffering from PAM, the malaria parasites utilise the developing placenta as a new niche for binding. Parasites causing PAM bind to chondroitin sulphate A (CSA) in the placenta, and the aim of this PhD study is to identify the protein mediating this binding and use it in a vaccine to induce antibodies which prevent PAM.

CSA adhering parasite lines were generated and a new and distinct PfEMP1 variant (*var2csa*) was found to be expressed in the parasites selected for adhesion to CSA and not in other non-adhering parasites. Most PfEMP1 molecules are highly polymorphic, but *var2csa* is carried by most parasites and well conserved. Presently, Ali is expressing *var2csa* in *E. coli*, insect cells and yeast to raise antibodies that can inhibit parasite adhesion to placental tissue.

Profile of a GMP doctoral student: Liverpool School of Tropical Medicine

Mr Themba Mzilahowa, College of Medicine/Wellcome Trust Laboratories, Malawi

After graduating from Chancellor College in 1994, Themba was awarded a scholarship by DFID to study agricultural entomology at Bunda College of Agriculture, University of Malawi. In 2000, he worked for a few months as a research assistant to Angus Spiers on a project investigating the ecological niches of malaria vectors in Malawi. This inspired him to pursue a career in vector biology.

His PhD commenced in September 2001, under the supervision of Drs Ian Hastings and Phillip McCall (at LSTM) and Professor Malcolm Molyneux (Director, Malawi-Liverpool Wellcome Trust Research Laboratories, Blantyre). His project is entitled 'Malaria in an area of intense transmission in Malawi: studies on transmission and genetic diversity of *P. falciparum* in the vector'.

After a few months of induction and training in Liverpool, most of 2002 was taken up with fieldwork, determining seasonal biting and malaria transmission rates at two rural sites in southern Malawi. Most of 2003 will be spent at LSTM for the second phase of activities, involving laboratory analysis of the specimens brought back from the field (investigating genetic diversity in *P. falciparum* in the mosquito). However, Themba returned to Malawi in June 2003 to assist in the teaching of the entomology assistants course run at the GMP Malaria Alert Centre.

Profile of a GMP doctoral student: London School of Hygiene & Tropical Medicine

Dr Evelyn Ansah, Dangme West District, Ghana

Evelyn was born and raised in Accra, Ghana. On completing high school she studied to be a medical doctor after which she worked for a few years at both a regional and teaching hospital in Ghana. During this time she developed an interest in public health and requested a district transfer. Shortly after her request, a position became available in Dangme West, where she has been working since 1996.



Evelyn Ansah. Photo: Cathy Bowler

On completing an MPH at the School of Public Health she decided that she would like to investigate further some of the public health issues she had come across in her work. She was awarded a PhD studentship in September 2002. She has spent some of her first academic year attending courses at LSHTM including extended epidemiology, statistics with computing, and statistical methods in epidemiology. Evelyn has now decided that her study will concentrate on modifiable financial barriers to achieving effective treatment for malaria.

This study will provide information on the relative importance of cost as a barrier to healthcare for children less than five years of age. An existing pre-payment scheme in the study area will be utilised to improve financial access to treatment for malaria for half of 2500 households who have not enrolled. The impact on severe anaemia, mean haemoglobin, hospital admissions, and anthropometric indicators will be assessed among children six months to five years of age. Health service utilisation and morbidity will be measured.

Evelyn is married with two children who are currently being looked after by her husband with the help of her mother whilst she studies in London.

GMP Training Fellows

A number of African scientists have been awarded the title of GMP Training Fellow. These scientists, who are all working on GMP funded research projects, were selected as they demonstrated the potential to be excellent future researchers in their field. Along with the title comes funding from GMP for relevant training. Those studying for their PhD are linking their PhD research to that of the projects they are working on.

Gates Malaria Partnership Training Fellows		
Name	GMP Research Project	Training
Lesong Conteh UK/The Gambia		LSHTM PhD
Fred Matovu Uganda	An investigation of the economic and socio-economic determinants of the demand for malaria treatment	LSHTM PhD
Maurice Kong'ong'o Kenya		LSHTM PhD
Abadou Mbaye Senegal	Intermittent SP to prevent moderate/severe anaemia and low birth weight secondary to malaria in pregnancy	Statistics/ Epidemiology
Babatunde Imoukuede Nigeria	Phase IIb studies of heterologous prime-boost immunisation against malaria infection in the The Gambia	Distance Learning MSc Health Systems Management
Raphael N'guessan Cote d'Ivoire	Evaluation of new insecticides and long lasting treatments for nets and other materials used in vector control and personal protection	Distance Learning MSc Infectious Diseases

Research

The overall aim of the GMPs research component is the promotion of research in malaria endemic countries into new interventions against the infection. GMP is undertaking research of direct use to policy makers, clinicians and others involved in the management of malaria. Research projects are designed to complement those of other groups and to be as interactive as possible.

GMP Research Committee

To ensure the quality of research undertaken under the auspices of GMP all proposals are subjected to review by a Research Committee. The Research Committee has met 10 times since its inception in October 2000. The Committee is chaired by Professor Hazel Dockrell, Head of Department of Infectious and Tropical Diseases at LSHTM. The Committee has five further members from LSHTM and three external members, two from WHO Geneva and one from LSTM. Both representatives from WHO Geneva are from malaria endemic countries and bring substantial experience of research in malaria endemic countries.

The Committee is responsible for the allocation of \$9.15m. Principal Investigators (PIs), one of whom must be a member of the LSHTM Malaria Centre, initially submit a brief pre-proposal for consideration by the Committee.

To date the Committee has reviewed 42 pre-proposals, 15 of which were considered during 2002/03.

If the pre-proposal indicates that the research is of a high quality and falls within the GMP objectives the PI's are asked to prepare a detailed, full proposal for consideration. All full proposals are sent to a minimum of three external reviewers for independent review. Proposals are also sent to members of the EOC. The GMP Research Committee has considered 28 full proposals since inception. Ten new full proposals were considered by the Committee during 2002/03 (see table below).

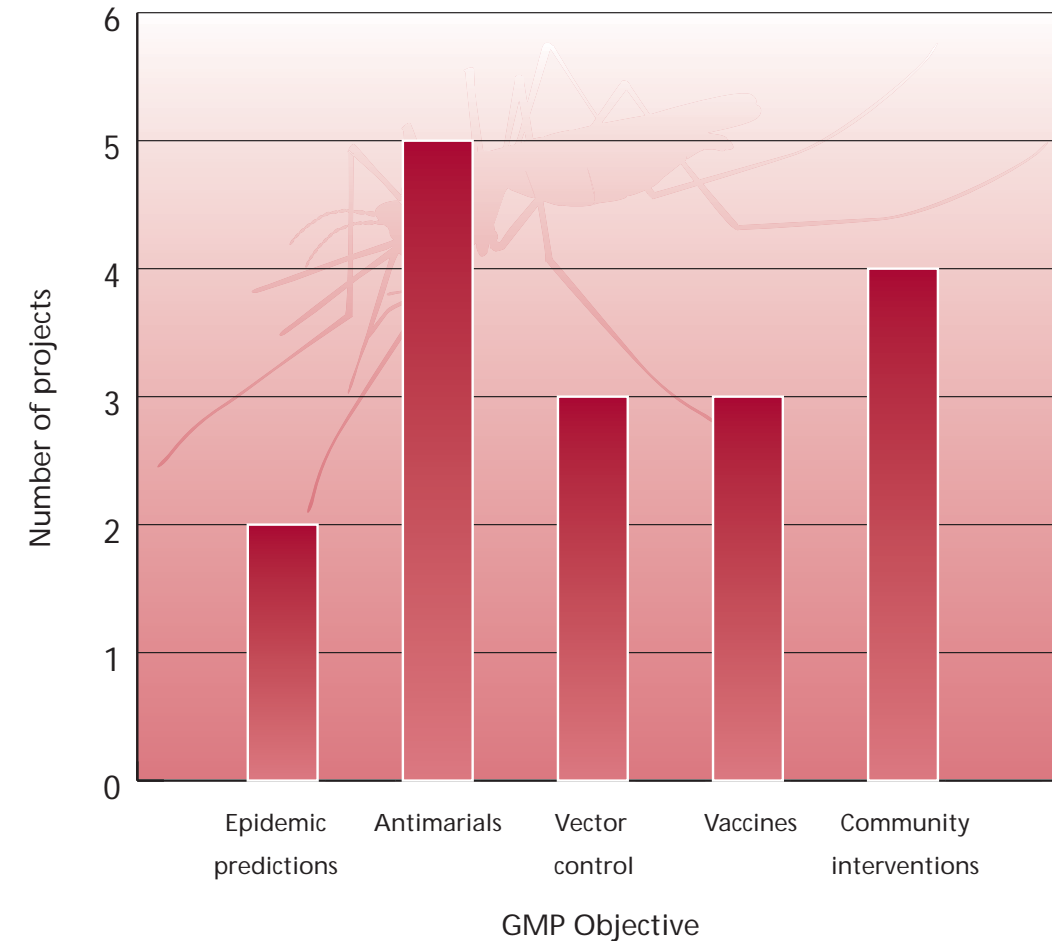
Since July 2002, 10 projects have been approved, with budgets ranging from \$82,514 to \$653,882. The Research Committee has approved a balanced portfolio of projects that cover the five GMP research objectives.

Full proposals received 2002/03

Date of Meeting	Received		Decision		
	New	Re-submitted	Approved	Deferred	Rejected
July 2002	1	0	0	1	0
Sept 2002	1	2	2	1	0
Jan 2003	2	4	4*	2	0
April 2003	6	2	4*	3	1
TOTALS	10	8	10	7	1

*3 for chairs action within one month

Projects by Research Objective



The following sections describe projects that have made substantial progress.

New systems for prediction and detection of malaria epidemics and use of GIS techniques in malaria control

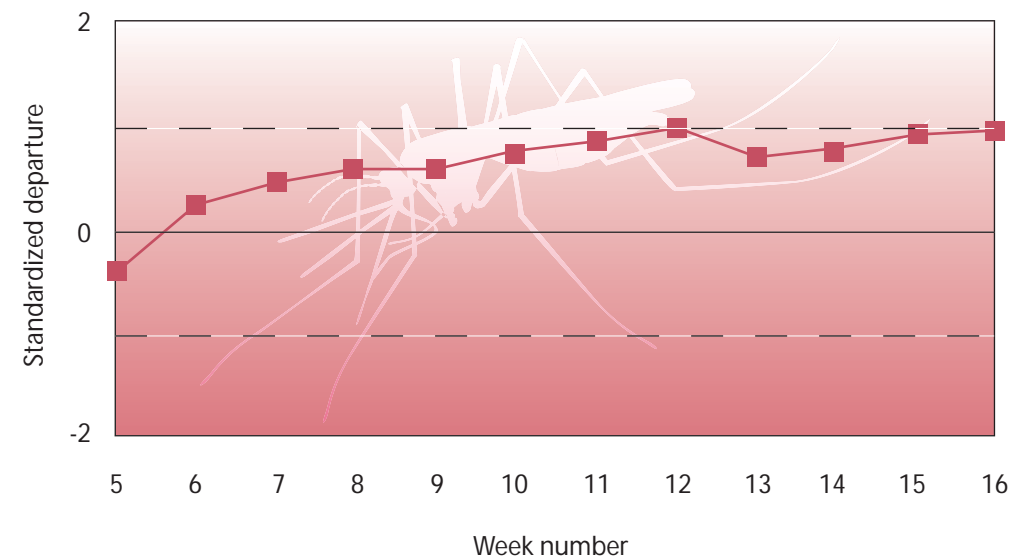
New systems for prediction and detection of malaria epidemics in the East African Highlands (HIMAL)

Principal Investigators: Dr Tarekegn Abeku (LSHTM), Dr Jonathon Cox (LSHTM)

Collaborators: Dr Menno Bouma (LSHTM), Dr Shak Hajat (LSHTM), Dr Simon Hay (Oxon), Dr Caroline Jones (LSHTM), Dr Peter Langi (NMCP, Uganda), Dr Jo Lines (LSHTM), Dr Sam Ochola (NMCP, Kenya)

African highlands have experienced a number of severe malaria epidemics in recent years, the impacts of which have highlighted the need for more effective systems for epidemic early warning and detection. The goal of the HIMAL project, launched as part of GMP in October 2001, is to develop and test such a system in the East African highlands. Specific activities include:

- development of new means of district-level surveillance for early detection of malaria epidemics using computer-based systems for organising and analysing health facility data and improving mechanisms for information dissemination; and
- development and validation of environmental models for predictions of epidemic risk based on surveillance and meteorological data, including remote sensing.



Standardised departure of outpatient malaria incidence from expected at Kaiboi Health Centre, North Nandi District, Kenya, 2003. This measure reflects the difference between observed and expected values for each week (in number of standard deviations), thus taking into account variability within a seven-year baseline data from which the expected values have been calculated.

A new surveillance framework was agreed in February 2002 at an inter-country workshop held in Kenya, which brought together relevant Ministry of Health and district health staff from affected areas. Needs assessments were carried out in four pilot districts, two each in Uganda and Kenya and sentinel sites were selected; 20 are now reporting to their respective districts on a weekly basis. Data entry comprises both simplified data entry and automated analysis modules including an in-built epidemic monitoring system. At four of the sentinel sites, weekly entomological studies are under way to monitor vector density and infection rates, and clinically diagnosed malaria cases are being tested for *P. falciparum* infection using rapid diagnostic kits. Automatic weather stations have been installed to continuously monitor temperature, rainfall and relative humidity. A link has been established with the European Space Agency to obtain historical and prospective remote sensing data.

The approach taken by HIMAL from the beginning was to ensure ownership of project activities and outputs by the national malaria control programmes (NMCPs) and district health management teams (DHMTs), who have committed themselves to incorporate the project into their national action plans.

Future plans include use of the various malaria transmission variables being measured longitudinally in order to formulate an effective model for area-specific early warning of epidemic malaria in highlands. NMCPs have already indicated their interest in extending the system to other epidemic-prone districts, and ways of doing this will be further investigated.



HIMAL technician taking blood sample from a patient (Bufundi Health Centre, Kabale District, Uganda). All clinically diagnosed patients are tested using a rapid diagnostics method. Photo: Tarekegn Abeku

Spatial analysis of drug and insecticide resistance: a joint LSHTM/LSTM initiative

Principal Investigators: Prof Janet Hemingway (LSTM), Dr Cally Roper (LSHTM)

Co-investigators: Dr Michael Coleman (LSTM), Dr Paul Coleman (LSHTM), Dr John Cox (LSTM), Prof Chris Curtis (LSHTM)

Collaborators: Dr Martin Akogbeto (West African MIM network co-ordinator, Benin), Dr Peter Mohloai (MIM Network, MRC Durban, South Africa), Dr Imbarani Moodley (MARA project, MRC Durban, South Africa), Dr Brian Sharp (MRC Durban, South Africa), Dr Tom Sukwa (WHO AFRO)

Malaria control in Africa relies on antimalarial chemotherapy and insecticide based vector control. In both cases successful intervention is threatened by the emergence and spread of resistance to the compounds used. Through collaborative research partnerships with Mapping Malaria Risk in Africa (MARA/ARMA), WHO AFRO, MRC Durban, and MIM networks, this joint LSHTM/LSTM initiative aims to extend understanding of the spatial distribution of resistance determinants in African parasite and vector populations at both high and low spatial resolutions, and the structural and temporal determinants of these distributions. LSHTM is taking the lead on drug resistance and LSTM is taking the lead on insecticide resistance.

Discoveries on the origins of antimalarial drug resistance in SE Africa (published prior to the start of the project) indicate that containment of the spread of resistance genes may be the key to prolonging the useful life of drugs in Africa. A study at LSHTM analysed flanking sequences around resistance genes and used this to define lineages of resistance whose distribution traces the extent of their spread. In this new project, their present day distribution will be described in the form of low-resolution pan-African maps. Analysis of these distributions in conjunction with historical data and empirical measurements will be used to examine whether there are certain regions of Africa through which resistance is characteristically more/less mobile. A training workshop was held at the MRC in Durban in June 2003 on the genetic analysis and quantitation of drug resistance in natural populations of *P. falciparum* to facilitate the training of personnel from partner institutions in South Africa and Tanzania who will contribute to this and other related projects.

The construction of databases has begun in order to describe the distribution of insecticide resistance in malaria vector populations at both high and low spatial resolutions, and to investigate potential determinants of these spatial distributions. An extensive literature search has been undertaken to compile all published data on insecticide resistance in Africa. A proforma and database based upon the MARA/ARMA format has been constructed collaboratively by LSTM and the MRC Durban that will allow the extraction of all georeferenced data from these publications.

Insecticide resistance data for *Anopheles funestus*, *An. arabiensis* and *An. gambiae* in sentinel sites in southern Africa is collected at MRC Durban as part of a MIM resistance monitoring project, the Lubombo Spatial Development Initiative and a Wellcome Trust GIS project. These data will be utilised in combination with a GIS technology to produce a high resolution map of the distribution of genetic determinants of insecticide resistance in southern Africa. Monitoring of these sentinel sites continues and further sampling sites will be established and monitored. The development of GIS and spatial analysis to describe and explain the spread of alleles associated with insecticide resistance within the vector population will be undertaken.



Staff from MRC Durban, South Africa with their new light box for scoring drug resistance SNPs. Photo: Cally Roper

Evaluation of new antimalarials and combinations of antimalarials

Evaluating the effects of combination therapy on the selection of drug resistance in *P. falciparum*, and the implications for public health

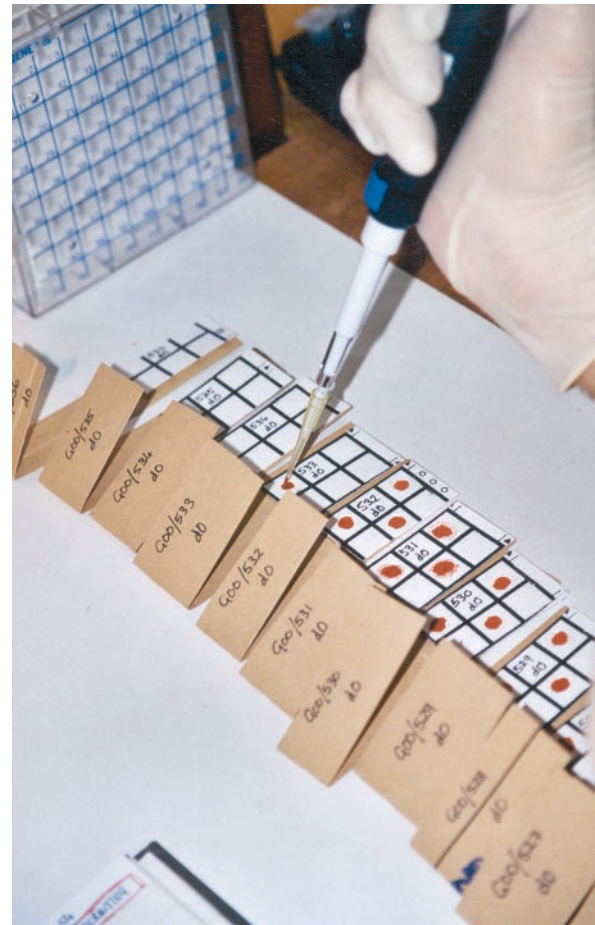
Principal Investigators: Dr Neal Alexander (LSHTM), Dr Ali Allouche (LSHTM), Dr Mark Rowland (LSHTM), Dr Colin Sutherland (LSHTM)

Collaborators: Dr Badara Cissé (IRD, Senegal), Mr Diadier Diallo (CNFRP, Burkina Faso), Dr Chris Drakeley (LSHTM), Dr Margaret Pinder (MRC, The Gambia), Dr Cally Roper (LSHTM), Prof Geoffrey Targett (LSHTM), Prof David Warhurst (LSHTM), Dr Chris Whitty (LSHTM)

The techniques of molecular genotyping of *P. falciparum* at loci known to be involved in antimalarial resistance are being used to evaluate the impact of combination therapy on the transmission of resistance in the context of controlled trials in The Gambia, Pakistan and Tanzania. Parasite DNA samples are being collected from patients prior to and after treatment and tested for the presence of resistance – associated alleles. Parasite DNA from oocysts obtained from the midguts of Anopheles mosquitoes are also being analysed to investigate the possible selection of drug – resistant strains at the time of mosquito infection.

In Farafenni, The Gambia, it has been shown that trophozoites and gametocytes emerging after treatment with chloroquine (CQ) may carry both the *pfcr-76T* and *pfmdr1-86Y* alleles associated with resistance. Prevalence of both *pfcr-76T* and *pfmdr1-86Y* in pre-treatment isolates from The Gambia have fluctuated over a 5 year period from 1998 to 2002. However, the prevalence of isolates carrying both these alleles has risen over the same period. This may be the result of co-selection, as there is significant linkage disequilibrium between these two genes. The effects on selection of resistance that occur when CQ is combined with artesunate are also being studied,

Analytical models are being developed to investigate the role of small sub-populations of resistant parasites, undetectable prior to treatment, in recrudescence of asexual parasites and in the emergence of gametocytes carrying resistance genes. New insights from these models into the impact of artemisinins on post-treatment recrudescence rates of both trophozoites and gametocytes of *P. falciparum* are of particular interest. Modelling of the clinical trial data confirms that artesunate has a direct killing effect on developing gametocytes, but indicates that this is tempered by a tendency to enhance the conversion from asexual to sexual stages.



Making blood spots for later DNA extraction in Farafenni.
Photo: Elisa Meier

Circulating gametocytes carrying drug-resistance alleles are frequently present among CQ-treated children in The Gambia who have made an adequate clinical response to treatment with no recrudescence of asexual parasitaemia. Using a membrane-feeding assay, these infections have been followed into the mosquito midgut. Results suggest sub-populations of resistant parasites expand rapidly in the host after treatment and go on to infect mosquitoes, thus transmitting resistance-associated alleles at a higher rate under drug pressure.

WHO has recently recommended that SP plus artesunate should become the new first line treatment for falciparum malaria in Iran, Pakistan, and Afghanistan. Baseline allele prevalences for *pfcr* and *dhfr* are being established in order to monitor any changes in prevalence after the new treatment policy is introduced later this year.

Logistic support and training in the techniques of resistance genotyping is being given to a number of projects within the LSHTM Malaria Centre and partner institutions in Africa and Asia. Scientists from Canada, Senegal, Burkina Faso, USA, Iran and Pakistan have or are being trained in these techniques.

Intermittent sulfadoxine-pyrimethamine (SP) to prevent moderate/severe anaemia and low birthweight secondary to malaria in pregnancy

Principal Investigators: Dr Gijs Walraven (MRC, The Gambia) and Dr Amadou Mbaye (MRC The Gambia)

Collaborators: Prof. Brian Greenwood (LSHTM), Dr Paul Milligan (MRC, The Gambia)

The frequency and severity of malaria infection is greater in pregnant women and in women who have just delivered (postpartum) than in non-pregnant women. There is good evidence that intermittent preventive treatment (IPT) is an effective strategy to decrease the risk of moderate/severe anaemia and low birth weight in primigravidae, but there is little information on its impact in multigravidae. There is no information on whether intermittent SP needs to be given throughout the year to pregnant women in areas where there is seasonal malaria such as The Gambia.

One component of this study will determine the efficacy of intermittent SP in multigravidae given throughout the year by means of a randomised, placebo-controlled trial involving 3000 multigravidae. By April 2003 nearly 2000 multigravidae had been recruited, with 90% follow up.

Iron and folate tablets are given routinely to pregnant women in The Gambia during clinic visits, to prevent nutritional anaemia. However, folate supplementation may reduce the activity of antifolate antimalarials such as SP. Thus, a second component of this study, conducted in 980 primigravidae, will determine the effect of giving folate supplementation at the same time as SP. By April 2003, nearly 500 primigravidae had been recruited, again with 90% follow up.

Haemoglobin testing. Photo: Gijs Walraven



An open-label, randomised four-arm efficiency trial of SP SP-amodiaquine, artemether-lumifantrine and amodiaquine-artesunate in mild-moderate malaria in Tanzanian children

Principal Investigators: Dr TK Mutabingwa (LSHTM, seconded from NIMR), Dr Christopher Whitty (LSHTM)

Collaborators: Prof Brian Greenwood (LSHTM), Dr Martha Lemnge (NIMR), Dr Robert Pool (LSHTM), Ms Virginia Wiseman (LSHTM)

Tanzania, in common with much of the rest of East and Central Africa, has a significant and growing problem with drug resistance to SP. It is, therefore, necessary to find a successor drug within the next few years. The aim of this study is to look at the operational effectiveness of three combinations of antimalarial drugs in an unsupervised outpatient setting in an area of Tanzania where there is known to be a high level of SP resistance. It is known that under the relatively idealised conditions of supervised efficacy trials, combination therapy is significantly more effective than treatment with a single drug. Artemisinin-containing combinations (ACTs) have received particular prominence as a potentially important combination. They have not, however, had extensive head-to-head studies in an operational setting in areas where resistance to standard monotherapy (CQ and SP) is high. Combinations which do not contain artemisinins (notably SP-amodiaquine) have proved effective in areas where there is some SP resistance. Additionally, one of the most important barriers to adopting artemisinin-containing combinations is cost. Whilst ACTs are not expensive drugs by global standards, they are generally more expensive than current treatment. This study, therefore, has economic and anthropological components that will explore the cost implications and acceptability of the drugs and combinations available, as decisions about which to deploy are likely to hinge as much on these as on drug efficacy.

The study began in July 2002. It has so far recruited 940 patients out of a target of just over 2000, and recruitment is on track to completion within the predicted time. The first 201 recruited were part of a pilot study to guide whether SP (current first-line treatment in Tanzania) or amodiaquine (current second line treatment) should be the monotherapy comparison arm. Day 14 parasite clearance was 74% in the amodiaquine arm but only 60% in the SP group. This high failure rate in the SP arm correlates with other studies in Muheza, so amodiaquine was chosen as the monotherapy comparison arm.



Dr Archie Hellar and Sister Devotha Anthony with a patient and her mother. Photo: Project Team

Treating malaria during pregnancy: a randomised trial of potential options for treatment in an area of high drug resistance in Tanzania

Principal Investigators: Dr Daniel Chandramohan (LSHTM), Dr TK Mutabingwa (LSHTM, seconded from NIMR) and Dr Christopher Whitty (LSHTM)

Collaborators: Prof. Brian Greenwood (LSHTM), Dr Martha Lemnge (NIMR)

A related problem for ministries, public health officials and clinicians in planning future drug policy for this region is that whilst pregnant women remain, after children, the group most vulnerable to malaria, there is relatively little published data on the efficacy and safety of the antimalarial drugs and combinations which are being considered for deployment. A second study in the Muheza district has, therefore, been planned and has received ethical clearance. This will look at amodiaquine-artesunate, amodiaquine-SP and chlorproguanil-dapsone (Lapdap™) in pregnancy, concentrating on efficacy and safety. Detailed planning for this trial was postponed by a few months until issues surrounding the safety of artemisinins in pregnancy had been resolved by an expert panel in WHO, and until chlorproguanil-dapsone has been licensed, anticipated in August 2003. The trial should begin in the autumn of 2003. A new ward has now been completed and equipped at Teule Hospital to allow the trial to be conducted safely without interfering with routine hospital activities, and the selection and appointment of staff has begun.

Evaluation of new methods of killing, repelling and controlling mosquitoes

Evaluation of new insecticides and long lasting treatments for nets and other materials used in vector control and personal protection

Principal Investigators: Prof. Chris Curtis (LSHTM), Dr Jo Lines (LSHTM), Dr Mark Rowland (LSHTM)

Collaborators: Dr Pierre Guillet (WHO Geneva), Dr Jean-Marc Hougard (IRD, France), Dr Traore Laminzana (Institute Pierre Richet), Dr Stephen Magesa (NIMR), Dr Caroline Maxwell (LSHTM), Dr Frank Mosha (KCMC), Dr Morteza Zaim (WHO Geneva)

The future impact of ITNs as a method of malaria protection may be undermined by the spread of pyrethroid resistant mosquitoes. GMP is, therefore, collaborating with the WHO Pesticide Evaluation Scheme (WHOPES), industry, and academic partners to identify and evaluate alternative insecticide products for use on nets or other types of materials. These include novel or existing insecticides that have the potential to overcome resistance, and long-lasting net treatments (LLN) that can withstand repeated washing over the lifetime of a net. To capture a broad entomological and epidemiological diversity, collaborative field work has been established with centres at Muheza in northeastern Tanzania (where *Anopheles gambiae* and *An. funestus* predominate), at Moshi near Kilimanjaro (where *An. arabiensis* is prevalent), and at Bouaké in Côte D'Ivoire (where pyrethroid resistant *An. gambiae* and *Culex quinquefasciatus* predominate). While activities in Côte D'Ivoire have ceased until the current political crisis is resolved, it was possible to carry out one promising evaluation (described below). In Tanzania insectaries for rearing mosquitoes, laboratories for testing insecticides, and experimental huts for evaluating ITN under controlled conditions are being constructed.



Collecting bed bugs for bioassay from rope beds in Muheza. Photo: Alex Asidi

Four of the major international companies – Dow, BASF, Bayer, and Syngenta – have submitted products for evaluation. Two of the major textile manufacturers – Vestergaard and SiamDutch – have submitted LLN and other materials for testing. The organophosphate insecticide chlorpyrifos methyl (CM) is showing particular promise as an alternative for use on nets. In London, in collaboration with Dow, ways of optimising the microencapsulated formulation and of enhancing residual life is being undertaken, while in Côte d'Ivoire CM has been successfully tested against resistant mosquito populations in experimental huts. In Muheza, CM was shown to be effective against the pyrethroid resistant bedbugs which have arisen as a result of exposure to pyrethroid treated nets over several years. With IRD a mixture of low doses of CM and pyrethroid worked well against pyrethroid resistant *An. gambiae* and *C. quinquefasciatus* mosquitoes that bear *kdr* or altered acetylcholinesterase resistance mechanisms.

Textile companies are vying to capture the potentially enormous LLN market. LSHTM is undertaking the important function of examining the veracity of company claims for their LLN products. Recent tests suggest that some LLN are partially but not yet fully wash resistant. Collaboration is being undertaken with WHO to evaluate factory impregnated polyethylene tarpaulins for use in refugee camps and natural disasters, and with BASF on the development of an LLN based on alphacypermethrin rather than the more usual deltamethrin.



Local *koroboi*-maker assembling the repellent lamp from recycled tin cans and bits of wire. Photo: Hans Jemet

Evaluation of a repellent-vaporising *koroboi* lamp for household level protection against malaria in rural Tanzania

Principal Investigators: Dr Ilona Carneiro (LSHTM), Dr Caroline Jones (LSHTM), Dr Jo Lines (LSHTM), Dr Mark Rowland (LSHTM), Dr Helen Pates Jamet (project leader)

Collaborators: Prof. Chris Curtis (LSHTM), Dr Martha Lemnge (NIMR), Mr Robert Malima (NIMR), Dr Caroline Maxwell (LSHTM)

Traditional kerosene lamps (*koroboi*) have been modified to vaporise volatile repellents for protection from mosquito bites in the early evening before retiring to bed. This repellent lamp (RL) showed good protection against nuisance biting mosquitoes in Dar es Salaam. The current GMP-funded study aims to improve the safety of the RL, assess its efficacy against anopheline mosquitoes and evaluate community acceptability of the RL in rural Tanzania.

Koroboi lamps are the most common light source in the study area, costing approximately \$0.10. They are generally used between 18:00h and 22:00h, although many are also used in the early hours of the morning, thus providing a potentially good complement to ITNs. A *koroboi* safety survey is being undertaken among approximately 400 households in the Muheza district.

Features needed to improve safety were identified, and one prototype was selected for further study. Households reported that it was easy to use, provided a good quality of light and was safer than the standard *koroboi*.

Entomological studies are underway using the Latin square design which involves rotating different treatments amongst houses and teams for humanbait mosquito catches. After comparison of different mosquito catching methods (human bait catch, light trap catch and a bednet-trap), the human bait catch was retained as the standard method for assessing the efficacy of repellents for this project. The efficacy of standard and locally available mosquito coils with the traditional method of burning leaves of a locally available plant (*Ocimum spp.*) was compared. Preliminary analysis indicates that all treatments tested, including burning *Ocimum spp.* leaves, significantly reduced the number of bites from *An. funestus* and *An. gambiae* compared to the control.

The efficacy of neem oil in the kerosene of the traditional *koroboi* and in the RL, and a range of concentrations of transfluthrin, a volatile pyrethroid, in the RL are being tested.

Clinical evaluation of the combined use of pyrethroid impregnated nets and plant-based insect repellents to control malaria in areas of early evening biting vectors (the Bolivian Amazon)

Principal Investigators: Dr Ilona Carneiro (LSHTM), Dr Nigel Hill (LSHTM).

Collaborators: Population Services International (PSI) Washington / Bolivia, Distritos de Salud Riberalta, Guayaramerin et Puerto Rico, Bolivia.

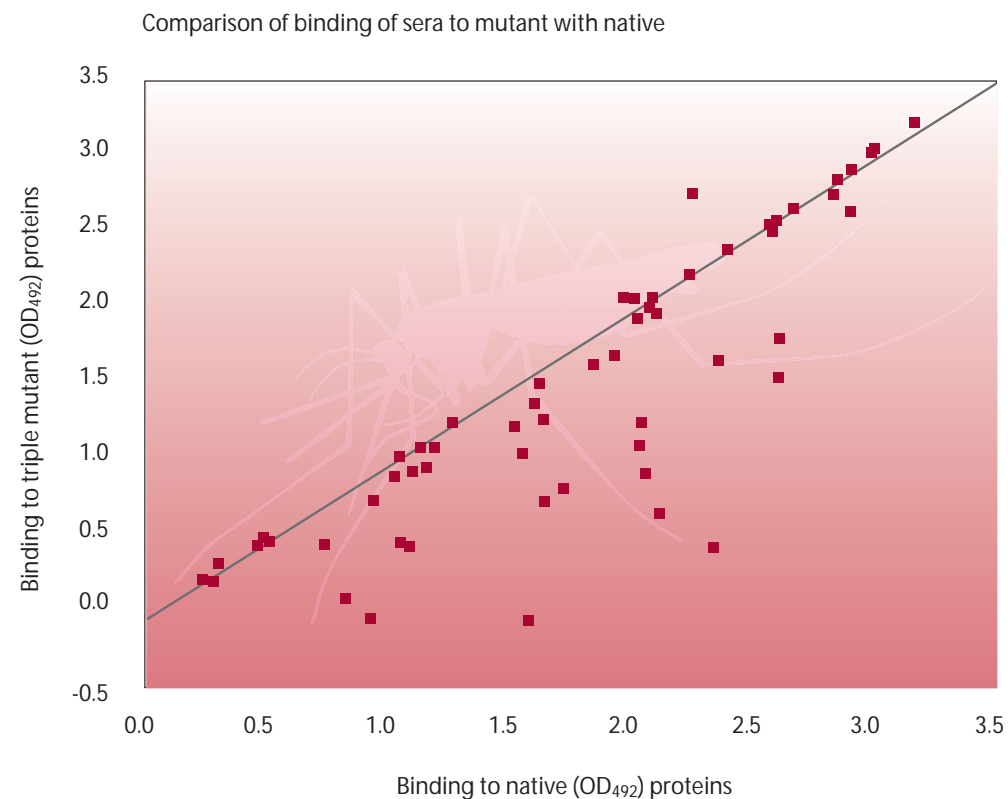
ITNs are one of the most successful means of reducing malaria in Africa where vectors tend to be late night, indoor feeders. In much of Central & Southern America, the major vectors such as *An. darlingi* and *An. albicans* have a feeding peak between 8-10pm, before most people retire to bed. In these circumstances it is unlikely ITNs alone will provide adequate protection. Supplemental use of insect repellents applied to the skin may be an effective method of personal protection in the hours between dusk and retiring to bed. It could also prove useful for those individuals working late or moving early into the forest where exophagic species are encountered.

This double blind, placebo-controlled study is designed to evaluate the efficacy of combined ITN and plant based insect repellent in reducing *P. falciparum* infection in the Bolivian Amazon in a region where ITNs alone are unlikely to be effective.



One of 11 study field workers from local Ministry of Health malaria team in Bolivia conducting a monthly survey of households, including use of *P. falciparum* specific dipsticks. Photo: Nigel Hill

Between 1991 and 1998, reported cases of malaria quadrupled from less than 19,000 to a peak of 75,000 annually in 1998. This study, based in the Amazonian Beni Region, where the majority of cases occur, has enrolled around 900 households (4,500 individuals) in rural villages and periurban areas. Baseline data were collected in March/April 2003 and currently are being evaluated. In April/May 2003, all individuals were issued with deltamethrin impregnated bednets and half given the active repellent, the other half a placebo. An earlier study had selected the natural plant-based repellent *Eucalyptus maculata citriodon* as the most suitable, giving 96% protection against local vectors for 4 hours. This plant can also be grown locally which may offer a sustainable, low cost source of repellent in the future. Monthly surveys, including use of *P. falciparum* specific dipsticks, are being conducted by local malaria control staff to allow assessment of efficacy by the end of the malaria season in the autumn of 2003.



Vaccine evaluation

In vitro/ex vivo assessment of vaccine-induced immunity to malaria

Principal Investigator: Prof Eleanor Riley (LSHTM)

Co-Investigators: Dr Patrick Corran (LSHTM on secondment from NISIB); Dr Brenda Okech (MedBiotech Laboratories, Uganda); Dr Amy Joynson-Hicks (LSHTM Sept 2001-Aug 2002); Dr James Todd (LSHTM)

Collaborators: Dr T Egwang (MedBiotech Laboratories, Kampala), Dr Anthony Holder (NIMR Mill Hill), Dr L Miller (Laboratory for Parasitic Diseases, NIAID)

The specific objective of this project was to investigate the specificity of naturally acquired antibodies to the malaria merozoite surface antigen PfMSP-1₁₉, part of the major surface protein complex of the merozoites of *P. falciparum*. This antigen has been shown to induce protective immunity when used as an experimental vaccine in animal models, but the evidence for its role in immunity to malaria in humans is equivocal. The hypothesis underlying the present study is that protection depends upon possession of antibodies of the appropriate specificity, and that some of the non-protective antibodies may interfere with those that do protect. The following have been used to begin to dissect the epitope specificity of human antibodies to MSP-1₁₉:

- peptide fragments of MSP-1₁₉;
- competition with *P. falciparum* MSP-1₁₉-specific monoclonal antibodies (MAbs) of defined function; and

- recombinant MSP-1₁₉ proteins in which key amino acid residues have been mutated.

Antibodies to MSP-1₁₉ have been shown to prevent merozoite invasion by binding to a site which prevents an essential proteolytic cleavage event ("secondary processing inhibition"); the function of these "inhibitory" antibodies can be "blocked" by antibodies of differing specificity that interfere with their binding. An extensive panel of recombinant proteins has been screened and three have been identified in which the binding site for "blocking" antibodies has been destroyed by site-directed mutagenesis whilst preserving the binding site for "inhibitory" antibodies. The ability of antibodies in sera from African children to bind to the mutant proteins and the native ("wild type") protein (see graph above) has been compared. Many of the sera contained antibodies that bound equally well to both the wild type and the mutated proteins (points close to the dotted line); it is suggested that these sera contain "inhibitory" antibodies and that these children should be relatively protected from clinical malaria and high parasitaemia. By contrast, a number of sera showed reduced binding to the mutant protein (points falling below the dotted line); it is suggested that these sera contain antibodies that are predominantly of the "blocking" phenotype and that these children would be less protected. When the clinical outcome in the two groups of children was compared it was found that children with "inhibitory" antibodies experienced significantly lower density infections than children with "blocking" antibodies.

These data indicate that inhibition of secondary processing of PfMSP-1 is a significant component of naturally acquired anti-malarial immunity and, there is now a series of simple *in vitro* assays that can be used to evaluate the antibody response to MSP-1₁₉ in clinical vaccine trials. These assays require validation with serum samples from vaccine trials.

Further work involves collaboration with Dr Brenda Crabb and Dr Rebecca O'Donnell (Walter and Eliza Hall Institute, Melbourne, Australia) to compare immunological indicators of protection with estimates of MSP-1₁₉-specific invasion inhibitory antibodies determined using novel chimaeric *P. falciparum*.

Phase IIb studies in heterologous prime-boost immunisation against malaria infection in The Gambia

Principal Investigators: Dr Kalifa Bojang (MRC, The Gambia), Prof Brian Greenwood (LSHTM), Prof Adrian Hill (Oxon), Dr Vasee Moorthy (Oxon)

Collaborators: Dr Tunde Imoukhuede (MRC, The Gambia), Gambia), Pauline Kaye (MRC, The Gambia), Sheila Keating (Oxon), Dr Paul Milligan (MRC, The Gambia), Dr Margaret Pinder (MRC, The Gambia), Dr Gijs Walraven (MRC, The Gambia)



Vaccinating a volunteer. Photo: Vasee Moorthy

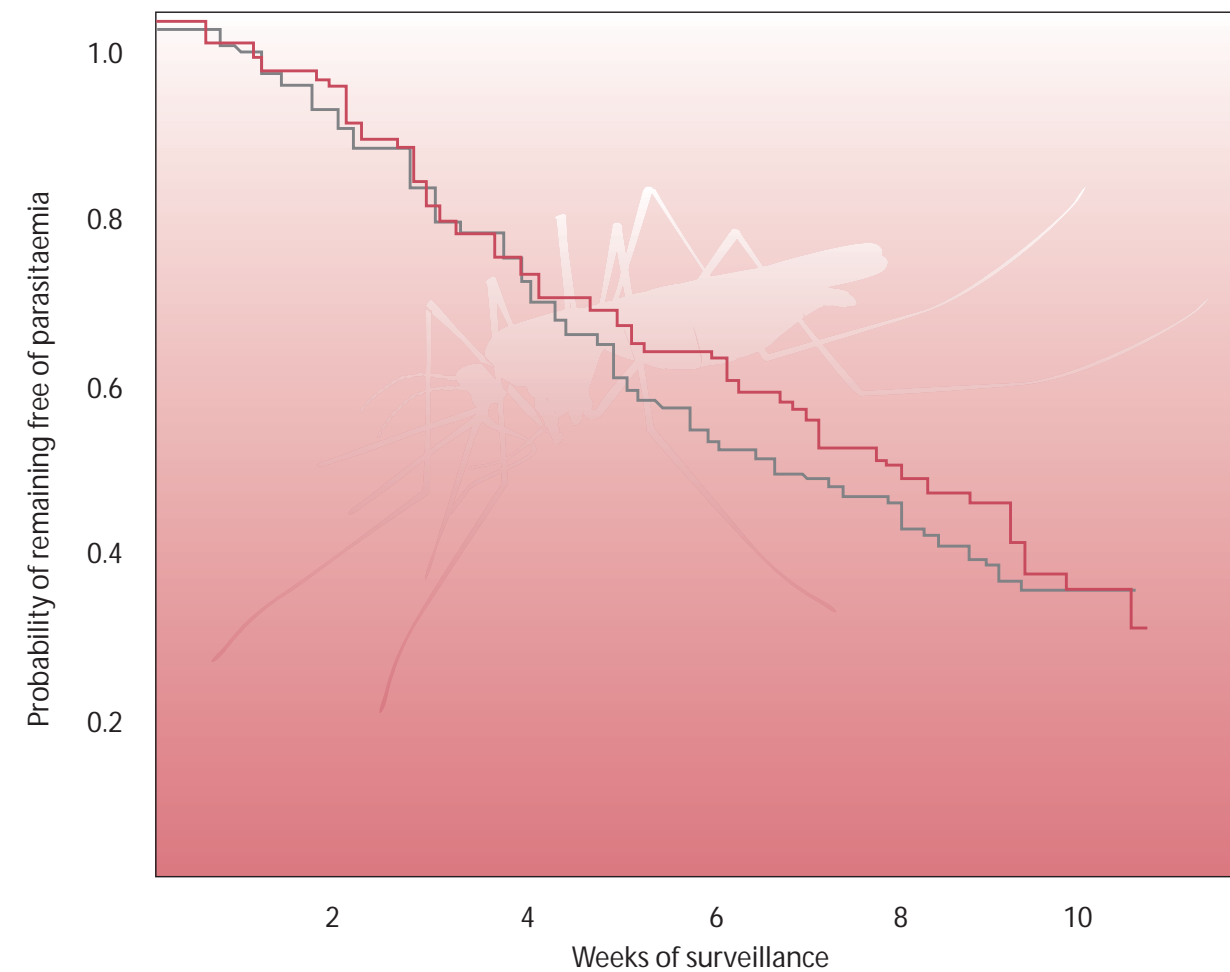
Many different approaches to the development of an effective malaria vaccine are being explored. One such approach is the administration of sequential DNA and virus-based vaccines, a strategy known as prime-boost immunisation. At Oxford University, this strategy has been explored using vaccines based on the antigen Thrombospondin Related Adhesion Protein (TRAP) linked to a string of epitopes. Initial experiments showed that vaccination using a DNA ME-TRAP vaccine followed by immunisation with the vaccine expressed in modified vaccinia Ankara virus (MVA ME-TRAP) led to the induction of strong T-cell responses against this antigen. In challenge studies volunteers immunised with the DNA ME-TRAP followed by MVA ME-TRAP had a substantial delay in the time to infection although all did eventually become infected. These results were considered encouraging enough to warrant a trial in subjects exposed to natural infection. Thus, a trial has been undertaken in semi-immune adults in The Gambia with support from GMP, the Wellcome Trust and MRC.

Three hundred and seventy-two Gambian men aged 15-45 years were randomised to receive either DNA ME-TRAP followed by MVA ME-TRAP or rabies vaccine. Two hundred and ninety-six men received three doses of vaccine and were followed up during the course of one malaria transmission season. No serious adverse events that could be attributed to the vaccination were observed and overall the vaccine was well tolerated. Subjects who received the malaria vaccines had a much stronger effector T-cell response measured by a gamma interferon ELISPOT assay than the control subjects who had received rabies vaccines.

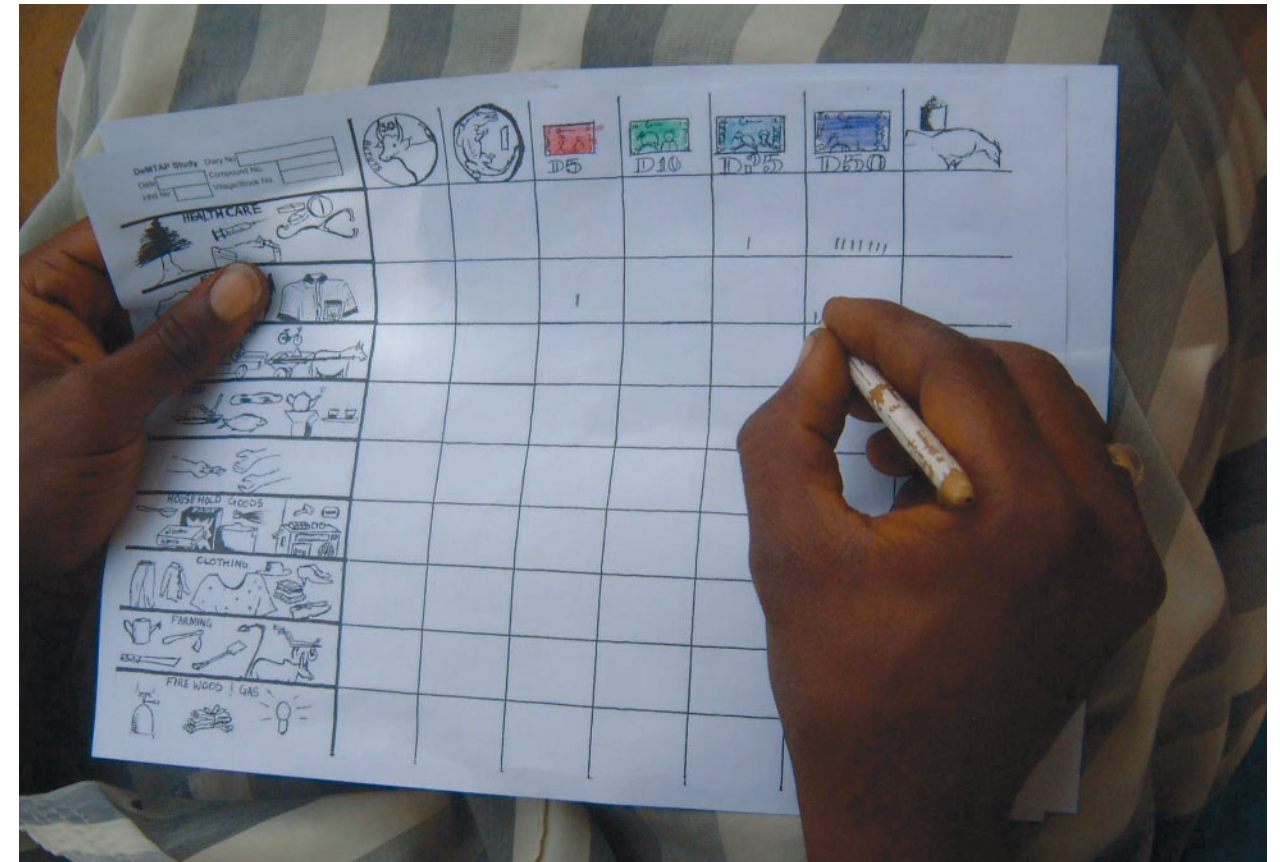
One hundred and seventy-one subjects developed malaria parasitaemia, 80/141 (57%) in the malaria vaccine group and 91/155 (59%) in the rabies group. The estimated vaccine efficacy against infection was 10% which was not statistically significant.

The results of this trial were disappointing as the vaccination strategy employed achieved the desired objective of a strong T-cell response against the target antigen. Further work is needed to determine whether this vaccination strategy might be more effective with other antigens or when given in combination with another vaccine that induces a strong antibody response.

Protective effect of prime-boost immunisation in volunteers*



* the data are unpublished and not citable without permission from GMP



Pictorial diary. Photo: Project Team

Evaluation of the impact of interventions at a community and health system level

An investigation of the economic and socio-economic determinants of the demand for malaria treatment and prevention

Principal Investigators: Dr Robert Pool (LSHTM), Dr William Mwengee (Regional Medical Officer, Tanga, Tanzania), Dr Warren Stevens (MRC The Gambia), Ms Virginia Wiseman (LSHTM).

Collaborators: Dr Brendan McElroy (Health Economist/Econometrician, University College, Cork), Prof Anne Mills (Health Economist, Director HEFP, LSHTM).

This study is investigating the factors influencing household demand for the treatment of malaria in Tanzania and The Gambia. Economic and anthropological methods are being used to explore why households make certain choices relating to malaria treatment and how this relates to the economic situation of the household and to various social and cultural factors. Particular attention is being paid to the way price, income, (perceived) quality of care/service, current health status, cost of access, ethnicity, religion, tribal affiliation, household size, marital status and other demographic and cultural variables influence consumption choices.

A sample of 1,600 households in both countries is being interviewed about their demand for different forms of malaria treatment, health care providers, the timing of treatment and the quantity of care consumed. A sub-sample of 300 households is being asked to record consumption and expenditure of drugs in diaries and to participate in a series of in-depth interviews exploring the reasons behind the entries in the diaries and the strategies used by households to cope with the associated cost of malaria. The field workers conducting the in-depth interviews are also observing at close hand why households make certain economic choices relating to malaria and how these relate to the economic situation of the household. Case studies of specific instances of febrile illness are being carried out and focus group discussions are documenting community perceptions.

The quantitative data from the household survey and the diaries will be used to develop econometric models of demand. To avoid selectivity bias, exogenous measures of price and quality will also be obtained from retail outlets and used in the econometric analysis. The quantitative results will be triangulated with the qualitative data to assess validity and to identify method-dependent differences in the consumption and expenditure data. All of the data will be combined to form a composite, in-depth picture of the demand for malaria treatment and healthcare more generally. This information will inform the design of current and future malaria treatment and prevention programmes and contribute to the development of local expertise in health economics.



Dr Eve Worrell with net sellers in Morogoro. Photo: Godlove Stephen

Scaling up ITN coverage in Tanzania: Understanding the contribution and limitations of the private sector

Principal Investigators: Dr Jo Lines (LSHTM), Prof Anne Mills (LSHTM)

Collaborators: Dr Salim Abdulla (Ifakara Health Research and Development Centre/NMCP Tanzania), Dr Kara Hanson (LSHTM), Dr Caroline Jones (LSHTM), Mr Godlove Steven (IHRDC) Dr Eve Worrall (LSHTM)

Private sector involvement will be necessary if the Abuja goals of 60% coverage of high risk groups with ITNs by the year 2005 are to be met. However, the commercial sector will not be sufficient alone, some form of targeted public subsidy will be needed to guarantee coverage of vulnerable groups.

The Tanzania ITN Implementation Plan is built on partnership with an exceptionally vigorous private sector, but also recognises the need for targeted subsidies. To this end, a national ITN discount voucher scheme (funded by the Global Fund to fight AIDS, TB and Malaria), delivered to pregnant women and young children through Mother and Child Health Clinics, is to be launched in 2003. Our research project aims to inform the scaling up strategies of Tanzania and other countries in two ways. Firstly, the progress of the commercial sector in nets and insecticide distribution in Tanzania and the limitations of its ability to achieve geographical penetration and high rates of coverage among vulnerable groups will be investigated. Secondly, the national voucher scheme for targeting subsidies on ITNs in terms of effectiveness in reaching the target group, sustainability and equity, and impact on the commercial market will be monitored and evaluated.

Retail audit and detailed household surveys are being carried out in selected districts. At the national level suppliers' and distributors' sales data and existing nationally representative household surveys are being used. PSI-Tanzania has received funding from DFID for continued

social marketing as part of the National ITN Strategy. An agreement has been reached with PSI-Tanzania to pool resources so as to extend the market monitoring from the 4 districts planned in our budget to a total of 10 districts. This will add significant value to our data.

A prerequisite to carrying out retail audit is a census of outlets in order to establish the "universe" for the audit. Preliminary analysis of census data from some of our selected districts has already been carried out and the retail audit tool (questionnaire) has been piloted and is now being used to collect data from these districts. The retail audit is on schedule to be up and running in all ten districts by July 2003. Development of a household survey tool is in early stages, with the data collection activities planned for November 2003.

Work on the voucher scheme evaluation is at an earlier stage due to delays in the launch of the voucher scheme. However, support has been provided to the pilot testing of the National ITN Voucher Scheme by carrying out a census of outlets and baseline ITN product availability survey (using the data collection instruments we have developed for our retail audit). A baseline household survey is planned before the launch of the voucher scheme in November 2003.

Malaria intermittent preventive treatment delivered to infants (IPTi) through the EPI system: community response to a new preventative measure and evaluation of the interactions with the EPI system

Principal Investigators: Dr Clara Menendez (Center for International Health, Hospital Clinic, Barcelona), Dr Robert Pool (LSHTM)

Collaborators: Dr Pedro Alonso, Center for International Health, Hospital Clínic, Barcelona, Spain & CISM, Maputo, Mozambique), Dr Martinho Dgedge (Dirección Nacional de Salud Comunitaria, Maputo, Mozambique), Dr Francisco dos Santos (Manhiça Health Center and Mozambican Ministry of Health), Dr Xavier Gomez-Olive (CISM & Center for International Health, Hospital Clinic, Barcelona), Dr Susanna Hausmann-Muela (Center for International Health, Hospital Clínic, Barcelona, Spain, and Centro de Investigação em Saúde de Manhiça (CISM), Maputo, Mozambique), Dr Eusebio Macete (CISM & Mozambican Ministry of Health), (Dr Joao Schwalbach, Facultad de Medicina, Universidad Eduardo Mondlane, Maputo, Mozambique), Prof Marcel Tanner, (Swiss Tropical Institute, Basel, Switzerland), Dr Arnaldo Timane (Manhiça Health Center and Mozambican Ministry of Health), Dr Ricardo Thomson (CISM, Manhiça, Mozambique)



Project ethnographers Zeca, Hortência, Simão and Luisa with their supervisor, Baslucas. Photo: Project Team

The effectiveness and safety of malaria intermittent preventive treatment for infants (IPTi), delivered through the Expanded Programme of Immunisation (EPI) has recently been demonstrated in a randomised controlled trial in Tanzania. However, new preventive health interventions such as IPTi can only be considered successful if they are also socially and culturally acceptable. An anthropological study linked to the IPTi trial in Mozambique is being carried out in order to investigate the social and cultural aspects of introducing IPTi into the EPI scheme. Of particular interest is the community understanding and acceptance of IPTi, the interaction between IPTi and EPI, and the influences of IPTi on people's preventive and treatment seeking behaviour for malaria and fever. Particular attention will be focused on peripheral health centre staff's understanding of and attitudes to IPTi and how this influences fever case management in infants. The expected outcomes of the study include understanding community and health staff responses to IPTi in order to contribute to policy guidelines for the implementation of IPTi in other settings. A start has been made on recruiting study participants and carrying out initial in-depth interviews (29 interviews completed by mid-June).

Research Initiative Fund

The research initiative fund provides seed money for pilot studies or to add value to existing studies through the provision of extra funds. \$305,526 has been awarded during 2002/03. A full list of the grants is shown in Annexe 4.

Infrastructure Programme

GMP is committed to providing the infrastructure for the training centres in Ghana, Malawi and Tanzania and to providing two malaria research laboratories in Tanzania.



Ghana building photo

Building works at the Ghana Malaria Centre (above) are now complete. Telecommunications and IT networking/Internet connections are currently being addressed.



Malawi building photo

The building works at the Malaria Alert Centre, Malawi (above) are also completed. Contracts have been let for telecommunications, networking and Internet connections. The training centre staff have relocated into their new building.



KCMC lab photo

The malaria research laboratory at KCMC (above) is just about complete. Trespa benching has been imported and installed by fitters from the UK. Although some equipment has been provided by GMP much needs to be done by KCMC's laboratory committee in the forthcoming year to ensure that the laboratory is equipped, staffed, and appropriately used.

A building for CEEMI is currently being erected at NIMR Headquarters, and is expected to be completed in November 2003. This building will also be occupied by the Tanzania's NMCP. A second malaria research laboratory is being built for NIMR at Bombo Hospital, Tanga, and is also expected to be finished by November 2003.

Knowledge into Practice

Several of the research projects described above bridge the interface between research and practice. For example the GIS epidemic prediction is helping government staff to improve their data collection systems in a way that could help to predict epidemics. However, two projects deserve special mention in relation to the use of research in determining drug policy – the Lapdap™ Public Health Group and the EANMAT.

Lapdap™ Public Health Group

Lapdap™ (chlorproguanil/dapsone), a new antimalarial which is effective against CQ and SP resistant malaria parasites, has been developed through a public private partnership between GlaxoSmithKline, WHO and DFID on the basis of preliminary work done under the auspices of the University of Liverpool. The Lapdap™ regulatory file was submitted to the United Kingdom's Medicines and Healthcare Products Regulatory Agency (MHRA) in October 2002 and received a letter of approvability in mid-2003. It is anticipated that final approval will be granted by the MHRA shortly (summer of 2003). The regulatory file was submitted to several African regulatory authorities in parallel with submission to the MHRA. Thus, it is anticipated that Lapdap™ will be available for use in several countries in Africa by the end of 2003. Obtaining regulatory approval is only the first step in ensuring that a new anti-malarial will be used to maximum effect. Thus, at the beginning of 2002, the Lapdap™ Product Development Team established a separate but overlapping group, the Lapdap Public Health Group (PHG) whose members have expertise in several aspects of social sciences as well as malaria control to address issues related to the introduction of Lapdap™ into malaria control programmes in Africa. The Lapdap™ PHG is organised under the auspices of the WHO Special Programme for Research and Training in Tropical Diseases (TDR) and is chaired by Dr Tom Sukwa, WHO AFRO. The Lapdap™ PHG is supported financially by GMP which is also represented in the membership of the group.



One of Lapdap's target groups. Photo: Trudie Lang

During 2002 and 2003 several meetings of the Lapdap™ PHG were held and its priorities were established. Currently, these fall into the following areas:

- **Information, Education and Communication (IEC).** Poor adherence could limit the potential publichealth benefit of a new antimalarial. To obtain data that would support the effective introduction of Lapdap™, a call for applications in relevant areas of research was issued through WHO TDR. Over 40 applications were received, covering areas such as users' perceptions of antimalarials, studies of health providers, and alternative methods to age in determining dosage. Two proposals have been funded so far and two more are under review.

- **Packaging.** Packaging can play an important part in ensuring that a new drug is used widely and in the correct dosage. Thus, the Lapdap™ PHG will consider ways of developing user-friendly (but inexpensive) therapy packs and information /educational messages to accompany the packaging selected. Therapy packs and information messages will be field tested. As Lapdap™ is likely to be used in both public and private healthcare systems, packaging and accompanying information material must be appropriate and cost-effective for both of these situations.
- **Pharmacovigilance.** Lapdap™ is likely to be licensed on the basis of efficacy and safety data collected in about 2,000 patients. This database is too small to exclude possible rare side effects, which may be seen in only 1:10,000, users or less. Thus, it will be important to monitor safety of Lapdap™ once the drug is introduced into routine use. Pharmacovigilance will be a core part of the work of the PHG. This will be done by collecting formal data from all phase 4 trials and, subsequently, by developing a system that could gather information on reports of possible side effects generated during the use of the drug within both formal and informal sectors. The PHG will work with other groups such as Roll Back Malaria and Essential Drugs and Medicines which have established pharmacovigilance systems to monitor the introduction of combination therapy.
- **Effectiveness.** The PHG will develop studies that will assess the effectiveness of Lapdap™ when used outside formal clinical trials in which a high degree of patient supervision is maintained and develop studies of the effectiveness of the drug in special groups such as pregnant women and HIV positive subjects. Assessing the safety and efficacy of the drug in pregnancy will be of high priority.

Although the Lapdap™ PHG will focus its efforts on the successful introduction of Lapdap™ into clinical practice it is hoped that many of the lessons that are learnt through doing this will be relevant to the introduction of other new antimalarials in the pipeline into clinical use in the most effective way.

EANMAT (www.eanmat.org)

The East African Network for Monitoring Antimalarial Treatment (EANMAT) was founded in 1998 to provide reliable and current estimates of malaria treatment efficacy. The network is composed mainly of staff from NMCPs of participating sub-regional Ministries of Health, supported by scientists and public health experts. EANMAT has participated and made significant contributions to antimalarial treatment policy review meetings in Uganda, Tanzania, Zanzibar, and Rwanda.

Dr Mutabingwa (GMP postdoctoral fellow) has been the Chairman of the Secretariat of EANMAT since its inception to date. He has chaired all meetings of the Secretariat which are held once every four months. In July 2002, he represented the Network at the inaugural meeting of the Central Africa Network for Monitoring Antimalarial Treatment, held in Yaounde, Cameroon. The Network has published one scientific paper in 2001 and another is in press. The Network has conducted two training workshops: one on data management in February 2002 and another one held in Zanzibar in October 2002 on the conduct of drug sensitivity testing. At both workshops, Dr Mutabingwa was a trainer/resource person. Although the Network is principally funded by the Department for International Development (DFID) of the British Government, the Secretariat is also responsible for soliciting funding from elsewhere to support other research relevant to antimalarial treatment. Under the guidance of the chairperson, EANMAT Secretariat has received additional funding from WHO AFRO and DANIDA.

More recently EANMAT has been involved in drug sensitivity studies at Mkuzi EANMAT Sentinel site, Muheza district and Dr Mutabingwa represented EANMAT at the Ministers for Health meeting of the Great Lake Zone Epidemiological Block, held in Kampala 24-28th June 2003. Three recommendations emanated from this paper and were later endorsed by the final meeting for implementation.

Publications

Part of the dissemination process is through publication in peer reviewed journals. Annexe 5 gives a list of all publications by GMP staff and students from July 2002 to June 2003.

Priorities for 2003/04

Priorities during the coming year include the following:

Capacity development and training

- Appointment of full-time directors at three training centres (Ghana, Tanzania and The Gambia) and strengthening of the staff and local steering committees of the four centres as recommended by consultants and the Expert Oversight Committee.
- Improved approval process for training proposals.
- Provision of more help for the training centres through the appointment of advisors on teaching technologies (LSTM) and quality assurance (LSHTM).
- Skills needs assessment for each training centre and the development of staff development programme. This will necessitate more frequent trainers meetings for key staff in the training programmes.
- Further development of each training centre's strategic plans.
- Completion of the training centre and laboratory building programme in Tanzania.
- Submission to the Gates Foundation of a supplementary proposal to support the recruitment of further GMP doctoral students.
- Development and implementation of a system for awarding GMP doctoral students follow-on grants.
- GMP doctoral students to be given the opportunity to attend the 2004 British Society of Parasitology meeting.
- Provision of the maximum support possible to the PhD students and postdoctoral fellows whose training programmes are now under way.

Research

- Careful evaluation of the 17 projects now supported by GMP through annual reports and by site visits from GMP administrative and scientific staff.
- Further exploration of ways in which individual projects supported by GMP might, if successful, be expanded beyond their initial period of funding into more extensive research programmes either on their own or as part of a new consortium following the model of the intermittent preventive treatment (IPT) consortium.

Knowledge into practice

- Difficulties have been encountered in finding an appropriate role for a member of GMP staff whose prime area of responsibility would be research into practice. However, during the coming year it is planned to establish a position in collaboration with the Malaria Consortium and a new drug sensitivity testing network in West Africa (WANMAT II). The person appointed to this post will have the responsibility of helping to see that research findings on drug resistance in West Africa are translated into appropriate national treatment guidelines.

Other

- The budget will be revised to take account of the new initiatives listed above.
- During 2003/4 discussions will be continued both within the partnership and with the Gates Foundation on the possible format for a submission to the Gates Foundation in 2005 of a proposal for continuation of funding to the Partnership.

Financial Issues

The financial statement for the 34 months to 30 June 2003 is shown on the following pages.

Budget

A revision of the budget was conducted in February/March 2003. Adjustments were made to reflect known activities at that time. Approximately 45% of the budget is expected to be spent in Africa. This includes approximately 80% of both the training proposals budget and the total research funds (excluding the LSHTM salaries), a proportion of the PhD support funds, all of the training centre/laboratory capital and equipment and training centre staff and equipment.

A number of crucial decisions were made at the meeting of the Expert Oversight Committee in May 2003 which have budgetary implications. These include recommendations for an appointment of a full-time Director to three training centres, recruitment of an educational technologist at LSTM, recruitment of a quality assurance advisor at LSHTM, the establishment of a working party on quality assurance and evaluation, and the provision of training for staff based at the training centres. Furthermore, the two malaria research laboratories will require financial support during their establishment period. The budgetary implications of the latter have not yet been fully assessed by the Partners, but a further review of the budget will take place in October 2003. It is expected that all these identified changes can be met from the existing budget.

Income

Despite low interest rates, the interest earned by the existing GMP funds has remained healthy. This has been due to careful cash flow management. To date \$3.7m has been earned in interest, giving a total income of \$43.7m.

Expenditure

\$13.8m has been spent to 30 June 2003. This is 32% of the current total income.

	Budget	Income/Expenditure covering the 34-month period to 30 June 2003		Commitments
	\$	£	\$	\$
Exchange rate \$1.43 = £1				
Income:				
Grant received		27,972,028	40,000,000	
Interest earned		2,620,134	3,746,791	
Total Income:		30,592,162	43,746,791	
Expenditure				
LSHTM Administration				
Admin & Computing Salaries	2,157,881	398,969	570,525	1,587,356
Conferences & Courses for Staff	65,065	8,487	12,136	30,000
Office Running Costs	324,610	82,962	118,636	205,974
Travel	517,660	98,172	140,385	377,275
Recruitment Costs	178,752	97,498	139,422	39,330
Rent	683,312	170,359	243,614	439,698
Insurance	125,000	20,000	28,600	96,400
EOC Meetings	661,496	78,871	112,786	548,710
Research Committee Meetings	28,473	7,796	11,148	17,325
Training Committee Meetings	500,047	100,594	143,850	356,197
Contingency	898,213	0	0	0
Overheads	3,817,324	606,962	867,956	3,046,505
Total Administration:	9,957,833	1,670,670	2,389,058	6,744,770
	23%			
Training				
London School of Hygiene & Tropical Medicine	331,794	61,758	88,313	100,000
Liverpool School of Tropical Medicine	421,357	132,656	189,697	231,660
Danish Bilharziasis Laboratory	422,480	119,103	170,317	252,163
Training Proposals	2,999,228	454,861	650,451	2,348,777
Total Training:	4,174,859	768,377	1,098,779	2,932,600
	10%			
Capacity Development and Knowledge into Practice Posts				
Salaries	600,000	36,855	52,702	547,298
Office Running Costs	300,000	1,553	2,221	297,779
Activities	1,085,318	1,707	2,441	300,000
Total Capacity Development and Knowledge into Practice Posts:	1,985,318	40,115	57,364	1,145,077
	5%			

	Budget	Income/Expenditure covering the 34-month period to 30 June		Commitments
	\$	£	\$	\$
Exchange rate \$1.43 = £1	\$	£	\$	\$
Research				
LSHTM Research Salaries	5,172,457	1,079,541	1,543,744	3,628,713
Research Initiative Fund	1,686,399	278,646	398,463	1,287,936
Lapdap™ Taskforce	1,422,876	495,019	707,876	715,000
GIS Collaboration	294,732	53,553	76,581	218,151
Other Research & Postdoctoral Awards	8,400,902	1,948,245	2,785,991	5,614,911
Training Fellowships	100,100	6,994	10,001	90,099
Total Research:	17,077,467	3,861,997	5,522,656	11,554,810
	39%			
Capital & Equipment				
Pharmacology Lab	294,634	136,038	194,534	100,100
Population Genetics Lab	313,935	212,432	303,778	10,157
Computer & Office Equipment (LSHTM)	1,169,134	133,813	191,352	100,000
Total Capital & Equipment:	1,777,703	482,283	689,664	210,257
	4%			
PhD Support				
Re-entry grants	850,000	0	0	850,000
London School of Hygiene & Tropical Medicine	759,616	245,829	351,536	408,080
LSHTM PhD research costs	474,102	218,814	312,904	161,198
Liverpool School of Tropical Medicine	894,227	351,462	502,591	391,636
Danish Bilharziasis Laboratory/ Centre for Medical Parasitology, Copenhagen	894,227	409,340	585,356	308,871
Total PhD Support:	3,872,172	1,225,445	1,752,387	2,119,785
	9%			
Africa Capital & Equipment				
School of Public Health – Ghana	417,042	287,478	411,093	5,949
College of Medicine – Malawi	541,856	254,358	363,732	178,124
NIMR – Tanzania	1,023,843	162,603	232,523	791,320
KCMC – Tanzania	538,722	304,871	435,966	102,756
MRC – The Gambia	94,810	22,899	32,746	62,064
Total Africa Capital & Equipment:	2,616,273	1,032,209	1,476,059	1,140,214
	6%			
Africa Staff & Recurrent				
School of Public Health	569,941	156,527	223,834	346,107
College of Medicine – Malawi	587,204	171,138	244,728	342,476
NIMR – Tanzania	571,643	164,276	234,914	336,729
KCMC – Tanzania	0	0	0	0
MRC – The Gambia	556,379	81,092	115,961	440,418
Total Africa Staff & Recurrent:	2,285,167	573,033	819,437	1,465,730
	6%			
TOTAL EXPENDITURE:	43,746,791	9,654,129	13,805,405	27,313,242
	100%			

Notes:

Income: Income of \$20m was received from the Bill & Melinda Gates Foundation in September 2000. \$19m was transferred into sterling at the time of transfer. A second transfer of \$20m was received in September 2001, when \$15m was transferred into sterling. \$1.43=£1 is the weighted average exchange rate at the time of these two transfers.

Expenditure

LSHTM Office Running Costs	£	\$
Photocopying & Printing	3,351	4,791
Annual Report Production	7,895	11,290
Telephone & fax charges	9,478	13,554
Post and courier charges	3,053	4,366
Stationery	4,165	5,956
Computer consumables	3,216	4,599
Meeting costs	6,015	8,601
Fund management fees	28,964	41,419
Miscellaneous	16,826	24,061
	82,962	118,636

Research Initiative Fund

This includes individual projects up to a value of \$28,600 (shown in Annexe 4), and costs incurred by research staff to attend conferences and meetings. Expenditure also includes seed money to cover some of the costs of the IPTi Consortium bid. It is hoped that this seed money can be recouped from the Consortium if the bid is successful.

Research grants – expenditure on individual projects	£	\$
Riley	42,208	60,357
Sutherland et al.	213,754	305,669
Mutabingwa, Whitty	116,356	166,389
Greenwood et al. (pregnancy)	173,350	247,891
Carneiro et al.	101,071	144,531
Lines, Mills	193,453	276,638
Wiseman	206,376	295,118
Abeku, Cox	241,353	345,135
Chandramohan, Mutabingwa, Whitty	59,571	85,186
Curtis, Lines, Rowland	73,204	104,682
Pool	40,907	58,497
Greenwood et al. (vaccine)	305,166	436,387
Hill, Carneiro	28,191	40,314
Rodrigues	24,859	35,548
Clarke	128,427	183,650
	1,948,245	2,785,991

Budget: The budgeted amount for computer and office equipment (LSHTM) includes a substantial building works contingency which will be reassigned if not required once the building works are completed. The budget will be revised towards the end of 2003 to account of decisions made by the Expert Oversight Committee in May 2003 once partners have accurately identified their funding needs. The percentage shows the proportion of a given budget category compared with the total.

Commitments: Commitments are defined as either an existing financial agreement with a partner institution or required to ensure that a committed activity can be carried out effectively. Currently 94% of the funds are committed.

Annexe 1: Committee Membership*

Expert Oversight Committee

Members

Dr Hatib Njie (WHO retired, The Gambia) CHAIR
 Dr Dan Colley (University of Georgia, USA)
 Dr Don de Savigny (Swiss Tropical Institute, Switzerland)
 Prof Wen Kilama (AMANET, Tanzania)
 Dr Jane Kengeya-Kayondo (WHO, Geneva)
 Dr Jean Francois Trape (IRD, Senegal)
 Prof Kazembe (MOHP, Malawi)
 Prof Francis Nkrumah (Noguchi, Ghana)

Representatives of WHO, DFID, MRC and the Gates Foundation are also invited

Attendees

Dr Tumani Corrah (MRC The Gambia)
 Prof Hazel Dockrell (LSHTM)
 Prof Brian Greenwood (LSHTM)
 Prof Janet Hemingway (LSTM)
 Dr Andrew Kitua (NIMR)
 Prof Isabella Quakyi (SPH)
 Dr Grace Malenga (CoM)
 Prof Niels Ørnbjerg (DBL)
 Prof John Shao (KCMC)
 Prof Geoffrey Targett (LSHTM)
 Prof Thor Theander (CMP)

Ms Cathy Bowler (LSHTM) Secretary

Research Committee

LSHTM Members

Prof Hazel Dockrell CHAIR
 Prof David Bradley
 Dr Peter Godfrey-Faussett
 Prof Paul Fine
 Prof Richard Hayes
 Prof David Mabey
 Dr Barbara McPake

External Members

Dr Kamini Mendis (WHO Geneva)
 Dr Ayo Oduola (WHO Geneva)
 Dr Stephen Ward (LSTM)
 Dr Alistair Robb (DFID, until April 2003)

Observers

Prof Brian Greenwood (LSHTM)
 Prof Geoffrey Targett (LSHTM)

Dr Amit Bhasin (LSHTM) Secretary
 *at 30 June 2003

Training Committee

Members

Prof Marcel Hommel (LSTM) CHAIR to 31/7/03
 Mr Said Al-Hussein (SPH)
 Dr Maru Aregemi (WHO Geneva)
 Dr Imelda Bates (LSTM)
 Dr Paul Bloch (DBL)
 Prof Ib Bygbjerg (CMP)
 Ms Angela Dawson (LSTM)
 Dr Anita Davies (LSHTM/WHO AFRO)
 Dr Fernando da Silveira (WHO AFRO)
 Ms Jane Edmondson (LSHTM)
 Prof Brian Greenwood (LSHTM)
 Dr Jasper Ijumba (NIMR)
 Dr Yaya Kassé (MRC The Gambia)
 Dr Grace Malenga (CoM)
 Prof Niels Ørnbjerg (DBL)
 Prof Geoffrey Targett (LSHTM) CHAIR from 1/8/03

Representatives of the NMCP of Ghana, Malawi, Tanzania and The Gambia are also invited

Ms Cathy Bowler (LSHTM) Secretary

Annexe 2: Key Staff*

Prof Brian Greenwood
 Prof Geoffrey Targett
 Mrs Cathy Bowler
 Dr Amit Bhasin
 Mr Brian Beard
 Ms Siobhán Renihan
 Ms Vivienne Dean

Dr Paul Bloch
 Dr Anita Davies
 Ms Angela Dawson

Mr Said Al Hussein
 Mr Kwabena Opoku-Mensah
 Ms Lynda Osarfo
 Mr Rockson Baah-Achamfour

Dr Grace Malenga
 Mr Vincent Kamange
 Mr Maxwell Chiundu
 Mrs Ronnah Kambalame

Dr Andrew Kitua
 Dr Jasper Ijumba
 Mr Obedi Ole-Kaondo

Dr Yaya Kassé
 Mr Balla Musa Joof
 Ms Nyah Polk

Dr Kalifa Bojang
 Dr Siân Clarke
 Dr Harparkash Kaur
 Ms Mojca Kristan
 Dr Wilfred Mbacham
 Dr TK Mutabingwa
 Dr Obinna Onwujekwe
 Dr Seth Owusu-Agyei
 Dr Robert Pool
 Dr Amabélia Rodrigues
 Dr Mark Rowland
 Dr Joanna Schellenberg
 Dr Christopher Whitty
 Ms Virginia Wiseman
 Ms Alison Yates

*at 30 June 2003

Director, GMP (LSHTM)
 Deputy Director, GMP (LSHTM)
 Manager, GMP (LSHTM)
 Assistant Manager, GMP (LSHTM)
 Computing Officer (LSHTM)
 PA to the Director (LSHTM)
 PA to the Deputy Director (LSHTM)

Technical Advisor (DBL)
 Capacity Development Co-ordinator (LSTM/WHO AFRO)
 Educational Advisor (LSTM)

Training Manager, GMC (SPH)
 Project Officer, GMC (SPH)
 Project Officer, GMC (SPH)
 Accountant, GMC (SPH)

Director, MAC (COM)
 Training Officer, MAC (COM)
 Assistant Training Officer, MAC (COM)
 Administrative Assistant, MAC (COM)

Director, CEEMI (NIMR)
 Deputy Director, CEEMI (NIMR)
 Manager, Joint Malaria Programme (NIMR)

Training Co-ordinator, CIAM (MRC)
 Assistant Training Co-ordinator, CIAM (MRC)
 Administrative Assistant, CIAM (MRC)

Clinician (MRC)
 Epidemiologist (LSHTM)
 Pharmacologist (LSHTM)
 Entomology Technician (LSHTM)
 Molecular Biologist/Public Health Specialist (LSHTM)
 Clinician (LSHTM/NIMR)
 Clinician/Health Economist (LSHTM)
 Epidemiologist (LSHTM/MOH Ghana)
 Anthropologist (LSHTM)
 Epidemiologist (LSHTM/Bandim Health Project)
 Entomologist (LSHTM)
 Epidemiologist (LSHTM)
 Clinician (LSHTM)
 Health Economist (LSHTM)
 Entomology Technician (LSHTM)

Annexe 3: GMP Doctoral Students Projects

Name	Research topic and home institution
Centre for Medical Parasitology, University of Copenhagen	
2001	
Pamela Magistrado	Identification and characterisation of <i>P. falciparum</i> variant surface antigens expressed by parasites causing severe malaria in children
Aziza Mwisongo	Intervention study aimed at improving advocacy of antimalarial guidelines at the community level <i>National Institute for Medical Research, Tanzania</i>
Ali Salanti	Defining the domains of the conserved PfEMP1 gene family which can be used in a vaccine against pregnancy-associated malaria
2002	
John Lusingu	<i>P. falciparum</i> immunoepidemiology among residents of communities with different malaria transmission intensity in north-eastern Tanzania <i>National Institute for Medical Research, Tanzania</i>
Liverpool School of Tropical Medicine	
2001	
Kofi Adasi	Investigations on insecticide resistance status and resistance genes/mechanisms in the main malaria vectors of Ghana <i>Noguchi Memorial Institute for Medical Research, Ghana</i>
Boniface Kalanda	Statistical evaluation of data on malaria in pregnancy and its consequences for the infant in rural Malawi <i>College of Medicine/Wellcome Trust Laboratories, Malawi</i>
Themba Mzilahowa	Malaria in an area of intense transmission in Malawi: studies on transmission and genetic diversity of <i>P. falciparum</i> in the vector <i>College of Medicine/Wellcome Trust Laboratories, Malawi</i>
Standwell Nhkoma	Role of parasite mutations in determining chloroquine resistance <i>College of Medicine/Wellcome Trust Laboratories, Malawi</i>
Daniel Wacira	Factors influencing re-treatment of mosquito nets with insecticides in malaria control programmes <i>AMREF, Kenya</i>
2002	
Lynette Ochala	Investigating the endocytic uptake of haemoglobin by <i>P. falciparum</i> during the erythrocytic cycle
Ruby Martin Peprah	The genetic susceptibility of hyper-reactive malarial splenomegaly syndrome in Kumasi, Ghana <i>Komfo Anokye Teaching Hospital, Kumasi, Ghana</i>
Rabia Mukadam	The impact of cotrimoxazole prophylaxis in HIV children on malaria treatment <i>College of Medicine/Wellcome Trust Laboratories, Malawi</i>
Happy Phiri	The relationship between <i>P. falciparum</i> var gene expression and sequestration to different endothelia <i>College of Medicine/Wellcome Trust Laboratories, Malawi</i>
Kamija Phiri	Iron deficiency in a population with high malaria and bacterial infection morbidity <i>College of Medicine/Wellcome Trust Laboratories, Malawi</i>

Name	Research topic and home institution
Danish Bilharziasis Laboratory	
2001	
Sheick Coulibaly	Relationships between the use of antimalarial drugs in pregnancy and <i>P. falciparum</i> resistance <i>Laboratoire National de Santé, Burkina Faso</i>
Anthony Mbonye	New approaches to delivery of malaria prevention interventions to pregnant women at community level in Uganda <i>Ministry of Health, Uganda</i>
Elisamia Nnko	Community perceptions, attitudes and practices in relation to chemical and non-chemical 'powerful' substances: implications for insecticidal malaria control strategies in NW Tanzania <i>National Institute for Medical Research, Tanzania</i>
2002	
Lucy Korukiiko	Influence of HIV infection on effectiveness of malaria chemoprophylaxis or intermittent chemotherapy on maternal malaria related morbidity and pregnancy outcome in Uganda <i>Uganda AIDS Commission, Uganda</i>
London School of Hygiene & Tropical Medicine	
2001	
Badara Cissé	A double blind randomised placebo-controlled trial to measure the potential of intermittent treatment with artesunate plus SP to reduce the malaria burden in sub-Saharan Africa <i>L'Institut de Recherche pour le Developpement, Senegal</i>
Diadier Diallo	Impact of long term implementation of insecticide treated curtains on the development and spread of resistance to chloroquine in Burkina Faso <i>Centre National de Recherche et Formation sur la Paludisme, Burkina Faso</i>
Robert Malima	Management of insecticide resistant mosquitoes in Tanzania <i>National Institute for Medical Research, Tanzania</i>
Harry Tagbor	A randomised clinical trial of amodiaquine (AQ), sulphadoxine-pyrimethamine (SP) used singly and in combination (AQ+SP) compared with chloroquine (CQ) in the treatment of falciparum malaria infection in pregnancy <i>St Theresa's Hospital, Kumasi, Ghana</i>
Eric Tongren	Antibody subclass switching in malaria: elucidating the factors regulating the production of IgG3 to <i>P. falciparum</i> Merozoite Surface Protein-2 (MSP-2)
2002	
Evelyn Ansah	A randomised controlled trial of the impact of improved financial access to healthcare on morbidity due to severe malaria and healthcare utilisation among children six months to five years of age in a malaria endemic area in Ghana <i>Health Research Unit, Dangme West District, Ghana</i>
Kalifa Bojang	A comparison of the efficacy of intermittent treatment with SP and insecticide treated mosquito nets to prevent morbidity in Gambian children treated for severe anaemia <i>MRC The Gambia</i>
Christine Clerk	Efficacy of SP and amodiaquine alone or in combination as ITP in pregnancy in the Kassena-Nankana district of Ghana: a randomised controlled trial <i>Navrongo Health Research Centre, Ghana</i>

Annexe 4: Research Initiative Grants 2002/03

Title of Study	PI (Host Institute)	Location of study	Value (\$)
The micro-spatial epidemiology of malaria in epidemic-prone and endemic areas in Western Kenya	Siân Clarke (LSHTM)	Kenya	22,608
Mosquito nets and equity in southern Tanzania: a qualitative comparison of three approaches to social marketing in five districts	Joanna Armstrong Schellenberg (LSHTM), Rose Nathan (Ifakara Health and Research Centre, Tanzania)	Tanzania	28,600
Insectaries for Moshi and Muheza, Tanzania	Chris Drakeley (LSHTM, Wellcome Trust), Robert Malima (NIMR, Tanzania), Frank Mosha (KCMC, Tanzania), Mark Rowland (LSHTM), Chris Whitty (LSHTM)	Tanzania	28,600
Provision of Internet facility via radio antenna at the cellular parasitology programme (CPP), Department of Zoology, University of Ibadan, Nigeria	Roseangela Nwuba (University of Ibadan, Nigeria)	Nigeria	8,580
Malaria management in a fractured society; treatment seeking behaviour in Kakuma refugee camp, Northwestern Kenya	Olivia Adong Lomoro (PhD student, LSHTM)	Kenya	7,186
Preparation for IPTi Consortium	David Schellenberg (LSHTM)	Global	39,662
Use and misuse of a discount voucher system as a subsidy for treated nets for malaria control in southern Tanzania	Joanna Armstrong Schellenberg (LSHTM), Adriana Tami (Swiss Tropical Institute, Switzerland and Ifakara Health Research and Development Centre, Tanzania)	Tanzania	21,450
Impact of long term implementation of insecticide treated curtains on the development and spread of resistance to chloroquine in Burkina Faso	Diadier Diallo (PhD student, LSHTM/CNFRP)	Burkina Faso	19,100
A double blind randomised placebo-controlled trial to measure the potential of intermittent treatment with artesunate plus sulfadoxine-pyrimethamine (SP) to reduce the malaria burden in sub-Saharan Africa	Badara Cissé (PhD student, LSHTM/IRD)	Senegal	28,600
A randomised clinical trial of amodiaquine (AQ), sulphadoxine-pyrimethamine (SP) used singly and in combination (AQ+SP) compared with chloroquine (CQ) in the treatment of falciparum malaria infection in pregnancy	Harry Tagbor (DrPH student, LSHTM/St Theresa's Hospital, Kumasi)	Ghana	28,600
Efficacy of sulphadoxine-pyrimethamine and amodiaquine alone or in combination as intermittent preventive treatment in pregnancy in the Kassena-Nankana district of Ghana: a randomised controlled trial	Christine Clerk (PhD student, LSHTM)	Ghana	28,600
A randomised controlled trial of the impact of improved financial access to healthcare on morbidity due to severe malaria and healthcare utilisation among children six months to five years of age in a malaria endemic area in Ghana	Evelyn Ansah (PhD student, LSHTM)	Ghana	28,600
Antibody subclass switching in malaria: Elucidating the factors regulating the production of IgG3 to Plasmodium falciparum Merozoite Surface Protein -2 (MSP-2)	Eric Tongren (PhD student, LSHTM)	London	15,340
Total Allocated by Director			305,526

Annexe 5: Publications

The following publications reflect work supported by the Research Committee of the GMP or work undertaken by GMP-funded staff during the period of the current GMP award from the Gates Foundation.

Development of new systems for the prediction and detection of malaria epidemics and use of GIS techniques in malaria control

Abeku TA, de Vlas SJ, Borsboom G, Teklehaimanot A, Kebede A, Olana D, van Oortmarsen GJ, Habbema JDF. Forecasting malaria incidence from historical morbidity patterns in epidemic-prone areas of Ethiopia: a simple seasonal adjustment method performs best. *Trop Med Int Health* 2002, **7**: 851-857.

Abeku TA, van Oortmarsen GJ, Borsboom G, de Vlas SJ, Habbema JDF. Spatial and temporal variations of malaria epidemic risk in Ethiopia: factors involved and implications. *Acta Tropica* 2003 (in press).

Evaluation of new antimalarials and combinations of antimalarials

Lang T, **Greenwood BM**. The development of Lapdap, an affordable new treatment for malaria. *Lancet Infect Dis* 2003; **3**: 162-8.

Sutherland CJ, Allouche A, McRobert L, **Ord R**, Leggat J, Snounou G, **Targett GAT**, and Pinder M. Genetic complexity of *Plasmodium falciparum* gametocytes isolated from the peripheral blood of treated Gambian children. *Am J Trop Med Hyg* 2002; **66**: 700-705.

Sutherland CJ, Allouche A, Curtis J, Drakeley CJ, **Ord R**, Duraisingh M, **Greenwood, BM**, Pinder M, Warhurst DC, **Targett GAT**. Gambian children successfully treated with chloroquine can harbour and transmit *Plasmodium falciparum* gametocytes carrying resistance genes. *Am J Trop Med Hyg* 2002; **67**: 578-585.

Sutherland CJ, Drakeley CJ, Obisike U, Coleman R, Jawara M, **Targett GAT**, Milligan P, Pinder M, **Walraven G**. The addition of artesunate to chloroquine for treatment of *Plasmodium falciparum* malaria in Gambian children delays, but does not prevent, treatment failure. *Am J Trop Med Hyg* 2003 (in press).

Von Seidlein L, **Walraven G**, Milligan PJM, Alexander N, Manneh F, Deen JL, Coleman R, Jawara M, Lindsay SW, Drakeley CJ, De Martin S, Olliaro P, Bennett S, Schimm M, Okunoye K, **Targett GAT**, McAdam KPWJ, Doherty JF, **Greenwood BM**, Pinder M. The effect of mass administration of pyrimethamine/sulfadoxine combined with artesunate on malaria transmission: a double blind, community randomised, placebo-controlled trial in The Gambia. *Trans R Soc Trop Med Hyg* 2003 (in press).

Von Seidlein L, Clarke S, Alexander N, Manneh F, Doherty T, Pinder M, **Walraven G**, **Greenwood B**. Treatment uptake by individuals infected with *Plasmodium falciparum* in rural Gambia, West Africa. *Bull World Health Organ* 2002; **80**: 790-6.

Von Seidlein L, **Greenwood BM**. Mass administration of antimalarial drugs. *Trends Parasitol* 2003 (in press).

Whitty CJ, Rowland M, Sanderson F, Mutabingwa TK. Malaria. *BMJ*. 2002; **Nov 23; 325 (7374)**: 1221-4.

Evaluation of new methods of killing, repelling and controlling mosquitos

Abdulla S, **Armstrong Schellenberg JRM**, Mukasa O, Lengeler C. Attendance bias limits the usefulness of a dispensary based case-control study for assessing morbidity impact of a treated bed net programme. *Int J Epidemiol* 2002; **31**: 175-180.

Armstrong Schellenberg JRM, Minja H, Mponda H, Kikumbih N, Mushi AK, Nathan R, Abdulla S, Mukasa O, Marchant TJ, Tanner M, Lengeler C. Short report: Re-treatment of mosquito nets with insecticide. *Trans R Soc Trop Med Hyg* 2002; **96**: 368-369.

Graham K, Mohammad N, Rahman H, Nazari A, Ahmad M, Kamal M, Skovmand O, Guillet P, Allan R, Zaim M, **Yates A**, Lines J, **Rowland M**. (2002). Insecticide treated plastic tarpaulins for control of malaria vectors in refugee camps. *Med Vet Entomol* 2002; **16**: 404-408.

Graham K, Mohammad N, Rahman H, Farhan M, Kamal M, **Rowland M.** (2002). Comparison of three pyrethroid treatments of top-sheets for malaria control in emergencies: entomological and user acceptance studies in an Afghan refugee camp in Pakistan. *Med Vet Entomol* 2002; **16**: 199-207.

Hanson K, Kikumbih N, **Armstrong Schellenberg J**, Mponda H, Nathan R, Lake S, Mills A, Tanner M, Lengeler C. Cost-effectiveness of social marketing of insecticide-treated nets in Tanzania. *Bull World Health Organ* 2003; **81**: 269-276.

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Mushi AK, **Armstrong Schellenberg JRM**, Mponda H, Lengeler C. Targeted subsidy for malaria control with treated nets using a discount voucher system in southern Tanzania. *Health Pol Plan* 2003 (in press).

Rowland M, Mohammed N, Rahman H, Hewitt S, Mendis C, Ahmad M, Kamal M, Wirtz R. Mosquito vectors and malaria transmission in eastern Afghanistan. *Trans R Soc Trop Med Hyg* 2002; **96**: 620-626.

Rowland M, Webster J, Saleh P, **Chandramohan D**, Freeman T, Percy B, **Durrani N**, Rab A, Mohammed N. Prevention of malaria in Afghanistan through social marketing of insecticide-treated nets: evaluation of coverage and effectiveness by cross-sectional surveys and passive surveillance. *Trop Med Int Health* 2002; **7**: 813-822.

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Wiseman VL, Phillips-Howard PA, ter Kuile FO, Nahlen BL, Vulule JM, Hawley WA, Mills A. The cost-effectiveness of Permethrin-treated bednets in Western Kenya. *Am J Trop Med Hyg* 2003; **68 (4)**: 161-167.

Webster J, **Chandramohan D**, Freeman T, **Greenwood BM**, Kamawal AU, Rahim F, **Rowland M.** A health facility based case-control study of effectiveness of insecticide-treated nets: potential for selection bias due to pre-treatment with chloroquine. *Trop Med Int Hlth* 2003; **8**: 196-201.

Vaccine evaluation

Allouche A, Milligan P, Conway DJ, Pinder M, **Bojang K**, Doherty T, Tornieporth N, Cohen J, **Greenwood BM.** Protective efficacy of the RTS,S/AS02 Plasmodium falciparum malaria vaccine is not strain specific. *Am J Trop Med Hyg* 2003; **68**: 97-101.

Salanti A, Staalsoe T, Lavstsen T, Jensen ATR, Sowa MPK, Arnot DE, Hviid L and Theander TG. Selective up-regulation of a single distinctly structured var gene in CSA-adhering Plasmodium falciparum involved in pregnancy-associated malaria. *Mol Microbiol* 2003 (in press).

Salanti A, Jensen ATR, Zornig HD, Staalsoe T, Joergensen L, Nielsen MA, Khattab A, Arnot DE, Klinkert MQ, Hviid L and Theander TG. A sub-family of common and highly conserved Plasmodium falciparum var genes. *Mol Biochem Parasitol* 2002; **122**: 111-115.

Evaluation of the impact of interventions at a community and health system level

Armstrong Schellenberg JRM, Nathan R, Abdulla S, Mukasa O, Marchant TJ, Tanner M, Lengeler C. Risk factors for child mortality in rural Tanzania. *Trop Med Int Health* 2002; **7**: 506-511.

Armstrong Schellenberg JRM, Victora CG, Mushi A, de Savigny D, Schellenberg D, Mshinda H, Bryce J, and Tanzania IMCI MCE baseline household survey study group. Inequities among the very poor: healthcare for children in rural southern Tanzania. *Lancet* 2003; **361**: 561-66.

Armstrong Schellenberg JRM. Tanzania IMCI Multi-Country Evaluation health facility survey study group. Healthcare for under-fives in rural Tanzania: effect of Integrated Management of Childhood Illness on observed quality of care. *Health Pol Plan* 2003 (in press).

Font F, Quinto, Masanja H, Nathan R, Ascaso C, Menendez C, Tanner M, **Armstrong Schellenberg JRM**, Alonso P. Paediatric referrals in rural Tanzania: the Kilombero District Study – a case series. *BMC Int Health Human Rights* 2002, **2**: 4.

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General

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Marchant T, **Armstrong Schellenberg JRM**, Edgar T, Ronsmans C, Nathan R, Abdulla S, Mukasa O, Urassa H, Lengeler C. Anaemia during pregnancy in southern Tanzania. *Ann Trop Med Parasitol* 2002; **96**: 477-487.

Miller L, **Greenwood BM.** Malaria – A shadow over Africa. *Science* 2002; **298**: 121-2.

Moore DA, Jennings RM, Doherty TF, Lockwood DN, Chiodini PL, Wright SG, **Whitty CJ.** Assessing the severity of malaria. *BMJ.* 2003; **Apr 12; 326(7393)**: 808-9.

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Tami A **Ord R, Targett GAT, Sutherland CJ.** Sympatric Plasmodium falciparum isolates from Venezuela have structured var gene repertoires. *Malar J* 2003; **2**: 7.



GATES MALARIA PARTNERSHIP

Partners

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Danish Bilharziasis Laboratory, Denmark

College of Medicine, University of Malawi, Malawi

National Institute for Medical Research, Tanzania

Kilimanjaro Christian Medical College, Tanzania

Liverpool School of Tropical Medicine, UK

London School of Hygiene & Tropical Medicine, UK

Medical Research Council Laboratories, The Gambia

School of Public Health, College of Health Sciences, University of Ghana, Ghana