Improving health, improving lives
MRC-funded research in Africa
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Front cover: Pateh Bah, a senior field worker for the MRC Laboratories, The Gambia, explaining how the use of insecticide-treated bednets can protect villagers from bites by malaria-infected mosquitoes. In 1989 the MRC Laboratories in The Gambia showed that the use of such bednets reduced children’s deaths from all causes by 63 per cent.

This page: Children in Kantong Kunda village, near Keneba, The Gambia.
Foreword

Professor Sir Gordon Conway KCMG FRS
Chief Scientific Adviser
Department for International Development

I warmly welcome this presentation of health research funded by the Medical Research Council (MRC) in Africa. As the Chief Scientific Adviser for the UK Department for International Development (DFID) part of my role is to ensure that science and technology fully inform UK development assistance efforts. The DFID’s work is focused on alleviating poverty and a key influence on our strategy is the UN Millennium Development Goals (MDGs) that were agreed by all the countries of the world in 2005. Health and the conditions which promote it are major themes across many of the MDGs, and science and technology have key roles to play in their attainment. As many African nations are not yet on course to achieve the MDGs by 2015, we need to work together to identify ways in which science and technology can help.

I see two particular areas where medical research – such as that funded by the MRC – is playing a key role in Africa. Firstly, the world currently does not have the range of medicines and vaccines required to achieve targeted gains in health and well-being in much of the developing world. Diseases such as AIDS, TB and malaria have a disproportionate impact on the poorest countries of the world, and a lack of investment in products targeting these diseases is a major problem. The development in recent years of public-private partnerships to bring together relevant expertise and investment to develop new medicines and vaccines is thus a very significant development. To ensure these partnerships establish an effective ‘pipeline’ of products, it is crucial that we have good biomedical research identifying potential candidates for development, good clinical trial facilities to establish the effectiveness of potential products, and good links with the communities that will use these products so that we take account of their needs and circumstances. Much of the work described in this publication is relevant to this task of product development, giving us real hope of more effective means for diagnosis and treatment of AIDS, TB and malaria and, through vaccine development, their prevention.

Secondly, where research is conducted in partnership with African scientists it will serve to develop research capacity in Africa. The G8 summit meeting in 2005 recognised the potential role of science and technology capacity development in supporting the economic development of Africa. There is real promise that investing in capacity for clinical trials and health product development will support not only the development of products for Africa, but also wider development goals. I see the development of centres of excellence in Africa, as highlighted in the Commission for Africa report, as a key element of development strategy, and greatly welcome the work of the MRC in supporting the establishment of African-led research institutions of global quality and significance. At the DFID we appreciate our increasingly close links with the MRC, marked by our joint funding concordat and our joint participation with the Wellcome Trust in the recently established UK Funders’ Forum for International Health. This publication highlights the first-rate work that is being done; first-rate not only in terms of scientific quality, but also in terms of its potential value in improving the health of many poor people living in Africa.
Our commitment to research in Africa

Introduction by Professor Colin Blakemore Chief Executive of the Medical Research Council

The MRC has been carrying out pioneering research in infectious disease for more than 90 years. Today we continue that tradition with well-planned programmes designed to alleviate some of the serious medical problems that bring daily misery to millions.

We conceived Improving health, improving lives in 2005, the same year in which the Commission for Africa did so much to make the public realise that much of the continent remains in the grip of devastating disease and crushing poverty. It builds on our response to the Commission, highlighting priorities, but it also carries the resounding message that although research has made a tremendous impact the job is far from done. And as you read on, you will encounter the thoughts and opinions of just a few of the many thousands of African people who are helping us to achieve our goal.

Three of the ambitious Millennium Development Goals adopted by the UN in 2000 refer directly to the need for medical progress – to reduce child mortality, improve maternal health and combat HIV/AIDS, malaria and other diseases. Furthermore, achieving the other five goals also depends on progress in alleviating the crushing burden of poor health in the developing world.

The scale of human tragedy that disease inflicts on sub-Saharan Africa has been clearly documented. According to the UN’s figures, some 26 million people living there have HIV. Experts predict that by 2010 every third child in Zambia will be an AIDS orphan. Malaria continues to claim the lives of up to two million people every year – most of these under school age – and one in four of all people suffering from TB lives on the continent. And all this despite the fact that health expenditure in this part of the world has risen sharply in the last 15 years.

Research is needed at all points in the discovery-to-evaluation ‘pipeline’. Continued investment in research and downstream development will lead to healthier, more productive lives for those suffering from appalling diseases – many of which we also experience in the developed world but on a much lesser scale. By the time you have read this brief introduction, at least two children will have joined the malaria mortality statistics. A sobering thought indeed.

It’s a challenging prospect to devise initiatives that will help us tackle diseases which have so far eluded scientific efforts. But the MRC is doing its best to meet that challenge and has demonstrated that there is light on the horizon. Here are just a few examples:

In The Gambia recent clinical trials have shown that children get extra protection against malaria from a new vaccine under development. In Uganda we are running trials to see if treating youngsters with an anti-infection agent called cotrimoxazole reduces deaths and morbidity from AIDS.

I am committed to the MRC doing as much as we can to develop and sustain excellent research in Africa. Our units will continue to discover, innovate and evaluate – whether it be for new and better vaccines or innovations like insecticide-treated bednets. Yet there will always be fresh challenges. For instance, we have known since the 1980s that insecticide-treated bednets are extremely effective in the fight against malaria. The challenge now is to find out why so many vulnerable people do not use such a simple device that can clearly prevent so much misery.

In an effort to combat Africa’s ‘brain drain’, we are successfully training and retaining the next generation of bright young scientists who work at our units in The Gambia and Uganda. I believe that in the coming years, African scientists will play an increasingly central role in the medical research that their continent so urgently needs.

In 2001 a global consultation of researchers and policymakers gave a clear message that the MRC should capitalise on UK and international commitment to reduce poverty and globalisation “as a rationale for increased investment in equitable research partnerships with other nations”. This surely still rings true today, which is why we maintain our commitment to the developing world, focusing mainly on Africa. We have just renewed our funding for the highly-productive research programmes of our units in The Gambia and Uganda, and we continue to fund UK universities investigating health problems in this part of the world. This is a vivid demonstration of our strategy of long-term investment in talented researchers and vital infrastructures.

Another important strand of our strategy is a commitment to international partnerships – for example the European and Developing Countries Clinical Trials Partnership,
Why research is essential

through which European and African countries are working together to develop new clinical methods to combat HIV/AIDS, malaria and TB in developing countries, including establishing a trials base for these diseases in Africa. In the UK, the MRC works closely with the DFID, with whom we have an agreement to coordinate health research policies in developing countries. Our other close UK partners in global research include the Wellcome Trust, the Economic and Social Research Council, the Royal Society of Tropical Medicine and Hygiene and leading UK universities.

As the pages that follow show, MRC scientists are making significant headway in the fight against some of the world’s most challenging diseases. There is still much work to be done, but we are committed to supporting the people of Africa in their quest for better health.

Africa’s health challenges and research needs have been well documented for many years now. In the 1990s, the term “the 10/90” gap was coined to express the acute global imbalance whereby developing countries experienced 90 per cent of the world’s major health problems, but received only 10 per cent of its resources for health research. Great strides have been made since then, through increased funding for global health research and for implementing the results of that research. Yet scientists still need to know much more about the mechanisms of health and disease in the developing world. And Africa’s armoury for fighting disease — the drugs, vaccines, diagnostics, services and implementation policies — is still almost bare. More high-quality research, including evaluation of new interventions in realistic settings, is essential to help rectify this situation.

Translating research into health benefits

The research and development work that produces a new drug or vaccine moves along a ‘pipeline’. The journey begins with basic discovery and initial testing, which is followed by further development and clinical evaluation before final implementation. The process can take many years. What’s more, it is often hugely expensive, with many initially promising discoveries eventually falling by the wayside because they don’t work well enough, are too costly or not safe enough. Public-private partnerships have stepped into the breech to provide the skills and investment needed to develop new treatments for diseases of the developing world such as malaria. Sometimes research for even relatively low-level interventions, such as education or the introduction of anti-malaria bednets, can be beyond the means of strained budgets and fragile healthcare systems.

An effective research strategy should encompass people, infrastructure, equipment and institutions, along with ethics, governance and good research management. It relies on clear theories and very robust research methods that can be validated independently by other researchers. A weakness in any of these links can cause a major problem.
Different types of research used to meet health needs

**Basic or ‘discovery’ research** generates new knowledge and can help to develop innovative treatments and technologies. It usually takes place in a laboratory or at a computer.

The human immunodeficiency virus (HIV) was identified through clinical and laboratory investigations in the early 1980s. A few years later basic and applied clinical research led to improved diagnosis and the first drugs to treat HIV/AIDS.

**Clinical research** uses groups of people, often patients, to answer questions about health and disease, through either their direct involvement or by studying tissue samples and data. Information gleaned from basic research is also added to this mix.

This type of research revealed that the clinical characteristics of HIV infection differ, to an extent, between Africa and industrialised countries. This finding helped researchers to create guidelines for clinical treatment. Clinical research also provides information about the side effects of new drugs.

**Social and behavioural research** can be used to test the acceptability of proposed health interventions, and to understand how and why they do or don’t work. It would be used, for example, to determine whether the promotion of condoms or vaginal microbicide gels is going to be acceptable. Improving people’s health involves more than biology. Scientists also have to consider what might be welcomed by one section of society but not another.

**Epidemiological research** is based on populations of people and may involve clinical measurements. It builds a picture of the spread and causes of disease, and shows whether public health measures are working.

Detailed epidemiology, along with clinical observation and statistical measurement, has been used to track the spread of HIV and identify populations most at risk. It has also highlighted the factors that helped the disease to spread or to combat it. Together these findings laid the foundations for testing interventions.

**Clinical trials** can be small-scale. Just a few people can begin the process of evaluating the efficacy, safety and acceptability of new drugs and vaccines.

Such trials were used to establish the fact that new microbicide gels, giving protection against HIV, did not cause bleeding or other complications and so would be suitable for evaluation in a population-based study.

But at a later stage, trials can involve hundreds or thousands of volunteers to build as realistic a picture as possible of the effects of a potential treatment.

**Population-based intervention trials** are used to test the strengths and weaknesses of health strategies, such as public education or mass vaccination, in entire communities.

These trials would be used to determine whether certain health programmes are suitable for the country where they will be used. They could be employed, for example, to establish what factors would encourage people to use antiretroviral therapy (ART). But they could also help to find out if the treatment would reduce the use of condoms.

**Health systems research** asks if and how particular public health programmes work and determines which components are effective and which are not.
Our strategy in action

Our research goals in Africa
The MRC’s health research programme in Africa is multidisciplinary, with a broad set of goals designed to meet the continent’s most pressing health needs:

- **Infectious diseases**: Africa’s greatest disease burdens are HIV/AIDS, other sexually transmitted diseases, tuberculosis (TB), malaria and, particularly in children, respiratory infections and diarrhoea.
- **Maternal health**: more high-quality research is needed to help prevent deaths of young women, particularly in low income groups.
- **Inequalities in health**: research should be aimed at helping the disadvantaged gain access to effective health interventions.
- **Health systems**: research is needed to provide evidence for healthcare and public health policy both regionally and internationally.

By exploiting the scientific opportunities and the research capacity that exists in Africa and the UK and through collaboration with African and UK-based research partners, we will:

- **Identify the causes and mechanisms** of diseases so that good health can be established and maintained.
- **Develop and evaluate** health interventions for prevention, diagnosis and treatment of disease.
- **Overcome barriers** that prevent the translation of research into clinical application, with benefits for healthcare and public health.

Our strategy for achieving our goals
We will support high-quality research by:

- **Funding competitive programmes and projects** that meet recognised standards in terms of research quality, ethics, relevance and value for money.
- **Awarding grants and personal awards** to UK universities and to MRC units and institutes in Africa and the UK.

We will develop and sustain research capacity in the UK and Africa by:

- **Attracting, developing and retaining** excellent scientists.
- **Providing and sustaining** the infrastructure and equipment that high-quality research needs.
- **Developing strong research institutions** with effective leadership, governance and management systems.
- **Sustaining a balanced research portfolio** in the UK and Africa.

By working effectively through partnerships internationally, nationally, regionally and locally, we can:

- Ensure that our research agenda is **relevant to Africa’s needs and deliverable**.
- **Coordinate** complementary research activities and strengths.
- Help to **translate** MRC research into policy and practice.
- Help our African partners to **develop and sustain** their own research capacity.

MRC investment in global research 2005

<table>
<thead>
<tr>
<th>Category</th>
<th>£’000</th>
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<td>Bacterial infections</td>
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<td>Insect vectors</td>
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<td>Malaria</td>
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<td>Nutrition</td>
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<td>Protozoa (excl. malaria)</td>
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<tr>
<td>Reproductive health</td>
<td>601</td>
</tr>
<tr>
<td>Viruses (excl. HIV/AIDS)</td>
<td>4,816</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>30,235</strong></td>
</tr>
</tbody>
</table>

Almost three-quarters of this research is carried out by MRC units and institutes; the remainder is conducted by MRC-funded scientists working in UK universities.
A long-term commitment

The MRC has built an impressive programme of health research in Africa over many decades, covering, among other things, infections and mother-and-child health. We first began working in Africa in 1913 — the year that the MRC was established in the UK — and we have had a strong relationship with local communities ever since. Here, we touch on some highlights of recent years, focusing on our programmes in The Gambia and Uganda.

Working with African scientists

Much of our global research programme is made up of the front-line work carried out by the MRC Laboratories, The Gambia, and the MRC/UVRI unit in Uganda (see page 8). Local and regional health needs play a large part in determining the research that they undertake.

Our African research units are forging collaborations with scientists worldwide, including those in other low-income countries. They place great emphasis on developing an internationally recognised body of talented African researchers, committed to improving health nationally and regionally. Not only do these researchers have strong links with UK university scientists, but their work is also complemented by research carried out at MRC units in the UK. For example, our National Institute for Medical Research carries out research into malaria and TB, our Clinical Trials Unit in London is involved in HIV research, and our Human Immunology Unit in Oxford is working on developing an HIV vaccine. In Cambridge, much of the work of the MRC Human Nutrition Research centre is directly relevant to our work in Africa. Discoveries by these units influence how our African units design and conduct their research. They have also had an impact on World Health Organization policy, particularly in the area of HIV and TB treatment.

The MRC Laboratories, The Gambia

Established in 1948, the MRC Laboratories in The Gambia are the UK’s single largest investment in medical research in a developing country. The unit has four main sites in The Gambia and one in Guinea Bissau. Together these provide the classic ‘bush, bench and bedside’ settings needed for high-quality laboratory-based and clinical research in Africa.

The unit has an internationally-recognised track record of research to prevent and treat diseases that have a major impact on the health of both the Gambian population and of millions of people throughout the tropics. There are programmes focusing on malaria and viral and bacterial diseases, along with work in immunology, genetics, epidemiology and public health and policy.

The Gambian people have an important claim on the unit’s research. For the research programmes to be approved by the government and the MRC Ethics Committee, they must benefit the Gambian people and the samples and data used in the work must remain in the country afterwards.

The unit also provides high-quality healthcare and employment for local people. This has helped the MRC to forge a strong relationship with the local community. The MRC’s relationship with the Gambian government is also highly valued. Members of the unit’s staff serve on boards and committees of the Department of State for Health and regularly meet their government counterparts. There is also a government/MRC scientific partnership committee, which meets annually to ensure that issues of mutual interest and importance are identified and addressed.

The UN Global Fund was set up in 2002 to fight AIDS, TB and malaria. The MRC and the Gambian government have together secured money from the fund to roll out antiretroviral therapy (ART) across the country. This has helped to stem the potentially catastrophic effects of HIV/AIDS in The Gambia. In addition, MRC research findings have informed The Gambia’s strategy for tackling HIV/AIDS through the National AIDS Control Programme and a new secretariat supported by the President.

Another close partner of the MRC is the Centre for Innovation Against Malaria. Funded by the Gates Malaria Partnership and set up under the auspices of the MRC unit with the support of the National Malaria Control
Our strategy in action
Improving health, improving lives

Programme, the Centre takes an innovative community-centred approach to tackling malaria.

At a local level the unit staff place importance on communicating directly with the public about health-related behaviour. A recent example was the development and distribution of a video guide designed to increase awareness of TB and of the benefits of diagnostic testing and treatment. Local people with experience of TB collaborated with MRC staff on developing the video. When the content was independently evaluated, audiences were able to identify the key messages. And the guide challenged some of their existing attitudes about TB, after which many expressed a desire to act on their new knowledge.

Research into HIV/AIDS
The prevalence of HIV/AIDS in The Gambia has doubled in recent years and although still comparatively low (1.2 per cent) compared to other African nations, there are around 2,000 AIDS orphans in the country. In 2003 it was estimated that 600 people had died of AIDS in The Gambia and nearly 700 were living with the virus.

Studying HIV/AIDS in The Gambia also has wider benefits for science. The virus that occurs there is HIV-2, an HIV subtype found almost exclusively in West Africans. People infected with this strain live longer and healthier lives than HIV-1 patients. As part of a study to understand why the two types of HIV differ, our Gambian researchers are examining why blood cells that offer protection (CD4 cells) decline much more sharply in people infected with HIV-1 than in those infected with HIV-2.
Dr Assan Jaye, who is looking at the molecular basis of immune responses in patients in both groups, said: “Surprisingly, the results showed that quantitatively there was no difference in immune responses between HIV-1 and HIV-2.” So, working with University College London, he investigated other components of the immune response such as the receptor repertoire for T cells, which help fight infection. Dr Jaye found there was a wider range of T-cell involvement in HIV-2 than in HIV-1. This hinted at the kind of qualitative responses that can differ and is providing new leads for treatments that could benefit people with either kind of HIV virus.

Research into tuberculosis (TB)

It is estimated that 2.5 million Africans have TB and that around one in five of those will die. The problem is being made worse by drug resistance and HIV infection, which is accelerating the rate of TB deaths.

However, a new vaccine treatment being tested in The Gambia is making good progress through its developmental stages. MVA 85A gives a boost to the tried-and-tested BCG vaccine and is one of the first new vaccines to treat TB for more than 80 years. Project leader Dr Helen McShane has discovered that the vaccine stimulates a much higher protective T-cell response in Gambians than in those who were tested in the UK. This may be because Gambians experience higher exposure to pathogenic and environmental mycobacteria. It is likely that the next stage of the study will move to vaccinating individuals who have latent TB infection.

The MRC/UVRI Uganda Unit

Medical research in Uganda has been an important focus for the MRC for many years. It began in the 1920s at the Ugandan Virus Research Institute (UVRI), a decade after the MRC (then the Medical Research Committee) was set up to find ways to tackle the problem of TB in deprived areas of London. Since those early years the UVRI has investigated a wide range of infectious diseases in Uganda, including yellow fever, various insect-borne viral infections and bubonic plague. The joint MRC/UVRI unit was set up in 1988, and its current focus is the renewed battle to control HIV/AIDS.

The Ugandan government responded quickly to the emergence of HIV/AIDS in the 1980s. When the scale of the epidemic became clear, it asked the British government to become a partner in its efforts to tackle the disease. The UK Department for International Development brought in the MRC, keen to harness its expertise in large-scale population studies and clinical trials, and in parasites, viruses and the immune system.

The United Nations AIDS programme, UNAIDS, estimated that around 26 million people in Africa were living with HIV in 2005. In Uganda, as in most parts of the continent, the picture is complicated and varies from region to region.

The UVRI and the MRC are using a wide variety of research tools to tackle the epidemic. Other research partners based at UVRI who are also working on HIV/AIDS include the Ugandan Rakai Health Sciences Project, the United States Centers for Disease Control and Prevention and the International AIDS Vaccine Initiative.

The MRC/UVRI unit’s basic science research programme at Entebbe studies changes in the virus, how it mutates and, by looking at their immune system and their DNA, why some people appear more resistant to HIV infection or to developing AIDS than others. At a population level, the MRC researchers are exploring the effectiveness of new preventive interventions, while in clinical settings they work with AIDS patients to help decide which methods of controlling the disease work best. All these findings will help to ensure that AIDS health policy works efficiently, not only in Uganda and across Africa, but also worldwide. And the MRC maintains a continuous dialogue with policymakers, including the WHO, so that its research results can inform health policy and practice as soon as possible.

MRC social scientists are also asking important research questions. For example, the success of ART in reversing the effects of AIDS prompts new questions about changes in patients’ behaviour. Are patients taking their drugs accurately, and if not, why not, and how can their adherence be improved? Does ART change the sexual behaviour of individuals with HIV infection and that of other people in the wider community? Does the chance of recovery reduce the stigma associated with the virus? And if so, does that affect the way being infected with HIV is seen by the rest of society?
“Each day around 14,000 people worldwide become infected with HIV”

United Nations AIDS Programme (UNAIDS)

MRC/UVRI research activities

Since it was founded in the late 1980s, the MRC/UVRI Uganda Unit has built a solid base in HIV research, with the tools and expertise to tackle difficult scientific questions. The current research programme includes population studies on the epidemiology and determinants of HIV transmission, the natural history of the infection and epidemiological, clinical, and social and behavioural studies related to interventions in rural and urban settings.

“The MRC/UVRI unit helps to generate information on how best to control the HIV epidemic and its consequences, both in Uganda and elsewhere in Africa, with the aim of informing health policy and practice,” says Dr Heiner Grosskurth, the unit’s Director. “Our key objectives are to develop and evaluate treatment strategies for AIDS patients, to find ways of preventing HIV transmission, to carry out basic science as part of HIV vaccine research for East Africa, and to monitor the AIDS epidemic over time.”

Building human defences against HIV/AIDS

The MRC’s newly built laboratories at Entebbe carry out research at the molecular level, using samples drawn from population groups recruited by the MRC. Dr Pontiano Kaleebu, head of the basic science programme at the MRC/UVRI Uganda Unit, here gives details of some of the work being carried out:

“We’re conducting a number of studies into HIV/AIDS, including one looking at HIV disease progression. In our cohorts we have identified individuals who progress very quickly to AIDS and others who progress very slowly. We are trying to find out if there are any immunological or virological factors that may determine the rate of HIV disease progression. The rate could differ so much because of the virus, the genetic make-up of the host, the immune response generated as a result of the infection, or there could be other environmental factors.

“We are also interested in people who are exposed to the virus but who remain HIV negative. So we are studying couples in which one partner is HIV infected but their regular partner is not. We are looking at the HIV negative partner to see if there are any factors, whether immunological or virological, that could make them resistant, and at the HIV positive partner to see if their virus has a particular characteristic that makes it less infectious.

“We’re also looking at the virus itself to understand its molecular characteristics, and to see how it infects cells and how it grows in culture. We hope to expand this work with international groups to look in detail at part of the virus ‘envelope’ – the outside part of the virus – to see if it has unique characteristics that could be a target for vaccine or drug intervention in the future.

“Also of great interest to us are people infected with one subtype of HIV who are then infected with a second subtype. If individuals with a good immune response go on to acquire a second infection with a similar or somewhat different strain of HIV, this will suggest that developing an effective vaccine will be very challenging.”

United Nations AIDS Programme (UNAIDS)
Highlights from the unit’s work in the last decade include:

- After investigating a large group of people in a rural population for a number of years, the MRC/UVRI unit showed in the 1990s that the rate of new HIV infections was falling, particularly among young sexually active people. This was the first time that researchers had been able to identify such an encouraging trend anywhere in Africa. It confirmed findings by the National AIDS Control Programme of Uganda that suggested a decline in the proportion of women with infection being seen at Ugandan antenatal clinics. And according to UNAIDS, a countrywide survey by Uganda’s Ministry of Health in 2004/05 estimated that seven per cent of adults were living with HIV – down from 15 per cent in the early 1990s. But while these findings suggest that the country has succeeded in controlling its HIV epidemic, scientists from the MRC and other partners are now warning that new epidemiological and behavioural data suggest that the past trends of declining prevalence may not continue in the future without a renewed focus on prevention.

- The MRC has found that during the early stages of an HIV epidemic, transmission is driven by risky sexual behaviour and is accelerated if other sexually transmitted diseases are prevalent. But in the later stages, the infection is transmitted through more stable partnerships. In these couples, the amount of virus in the infected partner is a major factor in transmission, as one of the MRC’s Ugandan research partners has shown. Researchers now believe that large-scale voluntary counselling and testing combined with preventive behaviour is vital in the fight to reduce transmission of the infection. In addition, the control of infection and treatment of other sexually transmitted infections remains an important strategy for high-risk groups.

- An MRC study showed that when poor commercial sex workers were helped to develop alternative incomes, it had little effect on their sexual risk-taking. This suggests that financial independence in itself is not a sufficient incentive for giving up prostitution, and that wider social norms need to change before women can negotiate safe sex.

- The use of cotrimoxazole, an easily available and affordable antibiotic medicine, has been shown by the MRC/UVRI unit and others to halve death rates among those infected with HIV. Today, the prophylactic use of cotrimoxazole has become general health policy in Uganda and elsewhere.

- The unit showed that when ART was given to people taking part in one of its studies, mortality fell by 90 per cent, and by even more in individuals whose immune suppression was not at the advanced stage. However, in those with highly advanced HIV disease, ART had far less impact on death rates. The WHO has published the findings as an example of what can be achieved if policymakers and health programme managers work together to promote and implement ART effectively.

For more examples of the impact that our African units are having on the continent’s health, please see “MRC research shaping health policy” on page 19.
Working with the people of Africa

To achieve our research goals for Africa, the MRC works with many different partners worldwide, from local villages and community groups to governments, other research funders, non-government organisations and international health agencies. They all play a part in ensuring that our research is focused, shared and able to have a positive impact on people’s health.

Understanding health by observing communities

Research involving people requires demographic information about the general population, including births, deaths and migration among villagers in rural areas. Our unit in The Gambia monitors such changes in the population through its Farafenni Demographic Surveillance System (FDSS). Set up in 1981, the FDSS covers 40 villages within a 32 km radius of the Farafenni research station – a total population of 42,891 people. Through continual surveillance in the region by local fieldworkers, it provides basic demographic information to inform new MRC studies. For example, the fact that the population is predominantly young, that there is a high rate of fertility and that there are around 80 men per 100 women.

Dr Momodou Jasseh, who supervises the fieldwork, says: “The Farafenni Demographic Surveillance System is a platform for conducting medical research. We have a team of workers that goes out into the field every quarter to ensure every household is visited at least once. We record if they are alive, if they have moved out of or into the area and eventually we wish to routinely monitor the body of disease.”

The FDSS has also influenced Gambian health policy by assisting research carried out for the National Impregnated Bednet Programme, which showed that child deaths from malaria can be reduced by up to 60 per cent through the use of chemically-treated bednets.

Similar observational studies are carried out by the MRC/UVRI Uganda Unit. At its remote field station at Kyamulibwa near Masaka, the General Population Cohort study has carried out a basic census of the region every year since 1989. Around 18,000 people live in Kyamulibwa, most of whom have agreed to take part. By having their blood tested, volunteers enable the researchers to monitor the HIV epidemic to see if it is getting better or worse, and to improve our understanding of current trends in the population. The study also provides new knowledge about the type and scale of other diseases in the population. Free medical care is given to people who agree to take part in the study, including free ART.

People who are found to be newly infected with HIV are asked to take part in the Rural Clinical Cohort, which studies the progression of HIV at defined time points and has been one of the key sources of information on how HIV progresses in individuals in Africa. The head of the Kyamulibwa station, Dr Lieve Van der Parl, explained that the team introduced antiretroviral therapies into the study in 2004: “Quite a lot of people have come forward in the past couple of years because they know that there is treatment available now. The volunteers are then seen every three months by a doctor, fill in a detailed questionnaire and have a clinical examination and lab tests to monitor their HIV progression. In this way, the volunteers gain good healthcare and the wider public benefits from our increased knowledge of the disease.”
All this work demands a large amount of statistical support. In 2005 the main unit in Entebbe received almost 300,000 data recording forms from all the studies taking place in Uganda. Not surprisingly, sophisticated systems are required to make sure that all this valuable information is received, entered correctly and stored safely.

**Africa’s genetic diversity: a unique resource for research**

Taken as a whole, the people of Africa are the most genetically diverse group in the world. As such, they are a uniquely valuable resource for medical science. By applying emerging new technologies to this extraordinary wealth of genetic data, scientists are about to explore one of the most exciting new areas of basic medical research.

The Fulani, a pastoral people distributed across West Africa are of particular interest to geneticists. They have long shown a reduced susceptibility to malaria, along with higher antibody levels than other groups in the same region.

Professor Dominic Kwiatkowski of Oxford University is working with research partners in The Gambia and other malaria-stricken regions of Africa, to examine the genes that control antibody response to malaria in the Fulani people. They have found early indications of the involvement of the interleukin-4 gene, a protein that stimulates the immune system. An understanding of these differences at the level of the genome could help scientists develop new approaches to preventing this life-threatening disease.

**Sharing genetic information across the globe**

Professor Kwiatkowski is analysing the DNA of thousands of malaria sufferers as part of the MalariaGen project. The knowledge gained will play a crucial part in the next phase of vaccine discovery. It also feeds into a much larger-scale ‘bioinformatics’ initiative known as the International HapMap project, which harnesses scientific partnerships throughout the world to create a global network of shared genomic information. The eventual aim is to help the international scientific community to understand differences between individuals, and to increase knowledge about the mechanisms driving diseases such as malaria. The contribution of Professor Kwiatkowski’s group highlights the importance of collaboration between research groups in Africa, and also between groups in Africa and other countries.

The HapMap project is mapping polymorphisms – tiny variations in DNA – in four major population groups, with the aim of mapping the entire extent of diversity in the human genome. Participating scientists all over the world are each contributing details of thousands of genomes. Their data are analysed centrally and then returned to the study site for the results to be published. The HapMap consortium promotes close collaboration between geneticists and ethicists at all stages of the study to make sure that any ethical issues – familiar or new – are identified and dealt with.

**Unlocking vital DNA information**

So far MalariaGen has worked closely with groups in Kenya and with the MRC Laboratories in The Gambia to collect data from more than 5,000 people with severe malaria.

Professor Kwiatkowski believes that the driving force behind this research is the strength of relationships between the community and the scientists. “The hard work is collecting the thousands of cases. Each time a child is admitted to hospital, someone has to treat them and complete a questionnaire. We now need to empower the people doing these studies to do the actual analysis,” he commented.

“We have to understand how we work as a community, how to respect the autonomy of individual sites and to make sure that the person working in an African hospital receives as much career advancement out of the publication of results as the principal investigators,” he adds.
The ambitious scale of the MalariaGen project makes human capacity and heavy-duty information technology pivotal to its continuing success over the coming years.

**Developing new interventions with the community**

More than half a million children worldwide died of AIDS in 2005. Most of them would have become infected during birth, which is why finding ways to prevent transmission from mother to child is an important part of the MRC’s research. Dr Van der Paré describes a current study at the Kyamulibwa field station in Uganda: “We give a drug called nevirapine to the mothers and a syrup of nevirapine to their newborn children. But as very few women give birth in hospitals here, we can’t rely on them getting the drug in hospital. Instead, we worked out a system through our counsellors and nurses, in which the mother takes her medicine home and takes it when she goes into labour. Then as soon as she has given birth a nurse or counsellor is called to the home to give nevirapine syrup to the baby in the first 48 hours.”

**Protecting women through microbicides:**

HIV infection occurs more frequently among women than men. The UN estimates that three-quarters of young people being infected with HIV are women between the ages of 15 and 24. During unprotected sex, women are twice as likely to become infected as men. And social inequalities between the sexes make the problem worse in Africa. So finding a way to address this problem has been a high priority for the MRC, with the favoured mechanism a vaginal microbicide gel designed to protect against STDs and HIV. First, the MRC carried out a number of safety studies, in collaboration with the St Francis Hospital in Nsanbya, Kampala and other research partners. PRO 2000, a gel that had already been shown to be safe in North America and Europe, was the chosen candidate. Now a trial of this gel involving 10,000 women is being carried out across South Africa, Tanzania, Zambia and Uganda, with funding from the DFID and the MRC. The study is part of the large-scale Microbicide Development Programme being co-ordinated by the MRC Clinical Trials Unit and Imperial College London.

Symon Wandiembe, the trial manager at Masaka in Uganda, says: “The problem is that to use a condom women have to negotiate with their husbands. Women in Africa have very low negotiating powers. Couples may find it easier to agree over using a microbicidal gel than a condom. It can be applied an hour before sex. It’s thought the gel works by killing the virus, blocking its entry into the body or by disrupting its attachment to the cells that carry it into the body system. In the laboratory, it was also shown to be effective against other sexually transmitted diseases such as herpes, chlamydia and gonorrhoea.”

At Masaka, the study is focusing on women at very high risk of infection because their regular sexual partner is HIV positive. Because it has been important to find out about the acceptability of the treatment, social scientists have also been involved. Counsellors help the volunteers to be open about their HIV status with each other, as Symon Wandiembe explained: “Because we are working with discordant couples – where only one partner is HIV positive – we make sure they receive counselling every month and that the use of a condom is recommended until we know whether or not the

Nurse counsellor Christine Musoke with John Nambale, a volunteer in the cryptococcal meningitis preventative trial being carried out at Masaka Regional Referral Hospital, Masaka, Uganda
gel is effective. We’ll follow them now for a minimum of two years. Since 2002, we’ve provided HIV counselling to more than 20,000 other people in rural communities. We treat sexually transmitted diseases and make home care visits for the sick. And we also educate people in the villages about how HIV spreads.”

Nora Nalwanga is taking part in the Microbicide Development Programme at a remote community health centre near her home. She found out about the trial through workshops in her village. She has already taken part in a four-week study of the acceptability of a placebo gel: “We were given instructions on how to use the gel so I haven’t had any problems with it. And my husband has had no difficulties either. We’re both happy with what the trial is trying to achieve. From the first study, we were told the gel might help in the prevention of HIV so I was very happy and decided to take part because I think it may help save lives in the future.”

**Targeting AIDS through DART**

Assessing the effectiveness and adaptability of the medical intervention being designed is an important aspect of health research. Some drugs and devices work perfectly well in one region but not in others.

ART is one such example. It has been used in developed countries for more than a decade, where it has significantly reduced the number of people who die of HIV-related diseases. But in Africa, the more basic health systems found in many parts of the continent could make its use logistically difficult and costly.

Laboratory support is generally thought to be necessary to monitor the use of ART correctly. But in rural Africa, laboratory services – with their technicians, scientists and sophisticated equipment – are often scarce. Millions of people in rural areas live out of their range. Since 2003, the DART (Development of ART in Africa) study has been exploring whether clinics in rural settings with limited lab support can treat patients effectively using ART.

MRC/UVRI Uganda Unit director, Heiner Grosskurth, explains how the study works: “The trial is being conducted at three sites: the MRC/UVRI Uganda Unit in Entebbe, the joint Clinical Research Centre in Kampala and the University of Harare, Zimbabwe. Of the 3,300 participants, 1,000 are enrolled at the MRC/UVRI unit. The study participants are allocated in an unbiased way (randomly) to either a group that regularly sees a doctor with sophisticated laboratory support or a group seen by a doctor without such support.

“DART is being funded by the MRC, the DFID and the Rockefeller Foundation. The study is monitored by an independent safety board, so that if one group was shown to be faring better than the other, the trial could be modified or stopped.”

Dr Diana Gibb of our Clinical Trials Unit in London is working on the ARROW study. This offshoot of the DART study is looking at ways of making ART more readily available to children. Two-thirds of the adults in the DART study are women, each one caring for an average of four children. Some of the children are known to be infected with HIV, but many are undiagnosed as yet. In Africa, the use of ART for children lags behind its use for adults, as the WHO reported in 2005. The challenges involved include diagnosing infection in young infants and being able to develop suitable, low-cost formulations of ART drugs for children to take in settings where resources, including laboratory support, are scarce.

“I believe that it is vital that families are closely involved in delivering ART to children, and not just for scientific reasons, but also to address logistical challenges such as drug-sharing in households. The ARROW trial will be investigating these and other questions, focusing on the children of families already participating in the DART study,” says Dr Gibb. The ARROW team are currently securing ART for the 1,300 children whom they plan to enrol in the trial. The MRC is funding the ARROW trial in partnership with the DFID.
Uganda’s success in managing its HIV epidemic is widely recognised. One vital ingredient in this success has been the emphasis placed on initiatives to empower local people with a sense of communal responsibility over managing the disease. For example, The AIDS Support Organisation (TASO), which was set up in 1987 by a group of infected individuals, and their relatives and friends. In the early days, the members met in each others’ homes to provide support and understanding about the disease and its effects. Over the years the organisation has been a crucial source of community-based activities and has given new hope to thousands. The MRC unit and TASO collaborate closely, with TASO helping the unit to gain access to consenting research volunteers and the unit providing TASO with laboratory support, drugs and medical care. This is an excellent example of how fruitfully community-based and research organisations can support each other’s work.

Currently four major joint studies by the MRC, TASO, the Ugandan Ministry of Health and other partners are underway. For example, in the town of Jinja on the shores of Lake Victoria, the MRC is working with TASO’s centre and the town’s hospital to investigate the rolling out of ART to clients under real-life conditions. Together they are comparing hospital-based delivery of the treatment with home-based delivery. The study will show whether field workers can provide ART in the community, saving patients’ time and transport costs. The researchers will also be looking at whether more regular and frequent follow-up by field workers can overcome the disadvantages of patients having less contact with doctors and nurses.

Kaloiesubula Muhammad, a DART trial volunteer, explained the benefits of the trial for him:

“I have been part of the DART trial since October 2003. I joined because the cells in my immune system were very low in number. My CD4 count was 99. I started here because I was a client of The Aids Support Organisation (TASO) and was HIV positive. I joined TASO because I had some diseases and they tested me for HIV. Then the trial came and I started treatment. I was very, very sick by that time.

“You can’t believe how I was. I was about 48 kilograms, now I am 70. DART has improved my life … now you can’t tell that I’m HIV positive and I am a responsible man. Now I can do my work and do what I like, but then I couldn’t lift a basin of water to bathe. I’m now a volunteer in TASO. I took a course in aromatherapy and reflexology and I can help other clients of TASO in their treatment. This has changed my life. I always take my drugs and come to see the doctors here.

“This work is not just helping me. It is helping the country. HIV here in Uganda is a real problem. We can’t do anything when we are sick, when we are poor, but when we are healthy we can do anything.”
Ethical aspects of research in developing countries

The MRC is committed to ensuring that the research it funds is carried out according to the highest ethical principles. For example, when working with human participants the researchers have a duty to alleviate suffering, to show respect for individuals, to be sensitive to cultural differences, and not to exploit the vulnerable.

Both international and MRC guidance for researchers working in the developing world stresses that before work starts, the research programme must be carefully reviewed by the appropriate ethical review bodies in the host country and the funding country. For example, for MRC research in The Gambia, the Gambian Research Ethics Committee and the ethics committee at the London School of Hygiene and Tropical Medicine review all research proposals. Particular attention is paid to researchers obtaining informed consent from study participants and, where culturally appropriate, from community leaders or senior family members as well.

Many developing countries do not yet have a well-developed capacity for ethical review of research. The MRC is working with international partners to help address this issue. We are a founder member of the Global Forum on Bioethics in Research, an informal partnership including the World Health Organization, the US National Institutes of Health and the Wellcome Trust. The MRC is also a partner in NEBRA – Networking for Ethics in Biomedical Research in Africa – which was set up to help 15 African countries improve their ethics review procedures to reach international requirements and so attract more clinical research programmes to help address the particular health needs of their people.

Forging a bond with the local community

The quality of the relationship between the investigators and the individual participants is an essential element in any high-quality, ethically sound research programme. Before beginning a study, the MRC works with volunteers to find out if it will be acceptable to local people. This involves explaining what, why and how of the clinical trial or study and the role of participants, as well as ensuring that all ethical requirements are met.

Pateh Bah is one of the MRC’s field workers in Farafenni, The Gambia, who works with the villagers of nearby Dutabulu where he is considered to be a trusted ‘part of the family’. Brought up nearby, he speaks the Fula language along with most other tribal tongues of the area. This means that Pateh can explain the intricacies of the research to volunteers and make sure they understand how to use new interventions. Our front cover photo shows him demonstrating the use of insecticide-treated bednets to a group of villagers.

At MRC Keneba in The Gambia, a team of ‘trekking’ midwives oversees births in and around the villages surrounding the field centre, and also deals with any problems during infancy. Fatou Sossey is the head midwife. She and her team of field workers and traditional birth attendants coordinate deliveries in rural areas where it is not unusual for women to have up to 15 babies. Typically for such rural areas, Fatou visits pregnant women as they work in the fields. She always brings treated bednets to protect the mothers and their children from mosquito bites, as they are the group most vulnerable to malaria.
Developing Africa’s research capacity

The World Health Organization (WHO) estimates that sub-Saharan Africa needs a million more professional health workers, and that 20,000 trained staff are lost every year to emigration. Africa is not only losing its doctors and nurses. Many graduates also leave the continent in search of higher pay. And Ugandan radio broadcasts advertisements urging young people to take up places at universities in industrialised countries. Talented scientists are also being enticed away, as a result of the lack of research facilities and career structures in Africa. This means that African research institutions cannot build up the number of skilled and capable scientists needed to compete internationally, so they have difficulty attracting funding.

Research capacity – the problems

Limited funding, poor equipment and minimal staffing levels leave few research institutions in Africa able to provide an adequate training structure for talented but inexperienced young scientists. Existing MSc and PhD schemes do not meet exacting standards and training is rarely an integral part of career development. This encourages an exodus of talent that leaves too few world-class researchers in Africa. Gifted scientists are often lured to institutions in industrialised countries where they stay after taking higher degrees. As a result most of the potential research leaders – those capable of running laboratories and major research programmes – continue to work outside Africa.

The resulting lack of critical mass of scientists leaves small research teams in Africa doing their best under difficult conditions. Not only do they lack strong links with other scientists working in the same field, but they also often lack the hi-tech equipment that is commonplace in industrialised countries. What’s more, their limited access to the internet can mean that they frequently miss out on learning about the latest scientific developments.

With the scales tipped against Africa, developed nations have far greater opportunities to exploit knowledge gained from research in this part of the world. The lack of collaboration between developing countries themselves causes an even greater imbalance.

Possible solutions

Strengthening the institutional structure in Africa can only be achieved through strong leadership, good governance and sufficient research funding. And to encourage staff to remain in, or to return to, a well-run research environment, they must be convinced that there is a solid career development scheme, that they will have access to modern scientific equipment, and that they will have a good opportunity to perform at a top level. In recent years, the MRC has welcomed a number of UK-trained Gambian researchers to senior posts at its Gambian unit.

Professor Tumani Corrah – Director of the MRC Laboratories, The Gambia – is working on a number of training initiatives to develop the skills of local scientists in an effort to encourage them to stay in the country. Professor Corrah says: “The unit has, since 2002, been implementing a locally adapted version of ‘Investors in People’ and spends around eight per cent of its budget on staff training.” The unit has established a Diploma in
Biomedical Sciences by distance learning with the University of Westminster. It is now in the process of establishing a BSc degree programme in collaboration with UK universities, and developing a fellowship scheme for graduates of the new University of The Gambia. In addition, Professor Corrah is developing an MSc course for Gambian students working at the National Malaria Control Programme, in partnership with Professor Steve Lindsay of Durham University.

The unit also has good links with the Royal College of Physicians through Professor Corrah’s presidency of the West African College of Physicians, and is planning a series of training courses for clinicians.

Even with good jobs and research support, African researchers find their main external links are with institutions outside Africa. AMANET, the Africa Malaria Network Trust, is one initiative addressing a range of human and institutional research capacity development needs in Africa. The European and Developing Countries Clinical Trials Partnership (EDCTP) is also promoting collaborations between developing countries.

“The MRC unit in The Gambia has both the scientific resources and expertise to play a significant role in building research capacity in Africa,” says Professor Corrah. Strong links between research institutions help to increase research capacity. National governments in Africa do not always recognise the centres of excellence in their own countries and so do not always provide the support they need to establish scientific networking. Organisations such as the EDCTP are working with the MRC and other partners to help forge these important links.

Providing a supportive environment The solutions to African research capacity are not going to be put in place overnight. However, there is increasing international recognition of the problem and agencies worldwide have expressed their willingness to help to improve the situation. The MRC will continue to be an advocate for developing African research capacity, and our African units will continue to play an important part in efforts to do so, as Dr Anatoli Kamali, who runs the MRC field station in Masaka, Uganda, explains:

“In most countries in Africa, certainly Uganda, there is a pool of scientists who need to be developed. It’s not just about salary. It’s about providing the right working environment. If a promising scientist wants to carry out an experiment or study he needs the means to do it. I think what has happened is that very bright scientists have been frustrated. They might not be able to get the necessary reagents, for example, or even have access to the internet. So they can’t compete favourably with a scientist with the same qualifications working in Europe.”

“At the MRC in Uganda, we set training goals for our young scientists and other staff. Exposure to scientific journals and papers is also important. Staff go to international conferences where they see how others work and ask ‘How can I improve?’ We have quite a number of papers which have been published and more are in the pipeline.”

Dr Anthony Kebba has resisted the brain drain. He was determined to acquire the vital scientific and health experience he needed – which he eventually gained with the help of the MRC unit at Entebbe in Uganda. Anthony started as a medical co-ordinator for a regional disease control programme. During his two years in this role he suffered the frustration of working in a very promising research area but without the funds or technology needed to help it bear fruit.

After moving on to work with AIDS patients, Dr Kebba realised that he needed further training and decided to opt for higher qualifications. Sadly he could not find an academic institution that had the funding and technology to provide the training and level of excellence he needed. He was then selected for the Rogers Research Fellowship, funded by and conducted at the MRC/UVRI Uganda Unit in Entebbe.

“I believe that the unit is a productive and well-supported environment in which to work,” said Dr Kebba. “However, although salaries are good, inflation and other unforeseen factors still keep eroding expectations of what can be achieved with money alone.”

Dr Anatoli Kamali, head of Masaka field station and project leader of the Microbicide Development Programme, Masaka
Here we show how MRC scientists’ research findings are having a positive impact on the health of Africa’s people. Our units will continue this progress by using interventions and technologies developed in Africa and other parts of the world. For example, MRC research teams are exploring the use of microbicide gels to prevent HIV infection and ways of adapting ART to meet the developing world’s needs.

**HIV/AIDS**

**Rolling out antiretroviral therapy:** In 2000, the Ugandan National Health Research Organisation carried out an analysis of health research institutions. Its report singled out the MRC Programme on HIV/AIDS as an example of research that has influenced policy and practice. A report published in 2005 by the WHO praised the efforts of sub-Saharan countries to meet its ‘3 by 5’ target of three million people worldwide receiving ART by the end of 2005.

Dr Kenya Mugisha, the Medical Superintendent at Masaka Regional Referral Hospital, described the process by which research findings influence government policy: “When new research or new technology is produced, the Ministry of Health in Uganda produces new guidelines. We have procedures to help disseminate new research findings. You get research results, you present them to people who are in charge of developing policies and guidelines and they share this information with our partner organisations, like the MRC or the US Centers for Disease Control and Prevention. A consensus is reached and then the policy comes into effect.

“As part of my work, I deal with the WHO and UNICEF frequently. I was told ‘If you want to see how something works, bring it to Uganda and if it works, it works.’ We’ve been leaders for lots of new technologies, treatment guidelines and even drugs. Take antiretroviral therapies. Uganda was one of the first African countries to get many people on to ART. I think we are in a good position to say whether something is going to work. We are on the ground, whereas the WHO is in Geneva.

“We now have a public health approach for scaling up the use of antiretroviral therapies. The Ministry of Health found the idea was attractive. We have been testing it here. Now we are moving it across Africa and people are saying, if you want to reach everyone with ART, this is the way to do it!”

The WHO reports that the number of people on antiretroviral therapies in sub-Saharan Africa increased eight-fold in two years, from 100,000 in 2003 to 810,000 by the end of 2005.

**WHO guidelines on ART use in children**

Inexpensive and effective medical supplies are not readily available in many parts of Africa. This is particularly true for HIV antiretroviral therapy. Because demand consistently outstrips supply, Dr David Dunn of the MRC Clinical Trials Unit is looking at deferring treatment while there is a low risk to the patient. Working with colleagues in London he evaluated the benefit of using total lymphocyte count (TLC) instead of the more commonly used CD4 cell count as a means of assessing the best time to give children ART. The findings showed that TLC predicts clinical progression almost as well as CD4 count. Where treatment resources are scarce, this finding has considerable practical implications. The WHO is incorporating this evaluation of TLC use into an update of its guidelines, *Antiretroviral treatment of HIV infection in children in resource-limited settings.*
Malaria

Helping Dutabulu village tackle malaria: the MRC has spent more than fifty years working from field stations in rural areas of The Gambia. During this time we have developed a strong relationship with local communities and an understanding of their beliefs and cultures. Both contribute greatly to the success of our research, as shown by the dramatic results achieved in Dutabulu, a village near Farafenni populated by the Fula tribe.

Bigi Jallow is the village chief. He says that the villagers work closely with MRC field workers over the problem of malaria. “Before the advent of the MRC the people here suffered a lot from malaria. But since they came there have been a lot of changes — the majority of the devastation caused by the disease has disappeared,” he says. “Before MRC work began here, if someone had malaria and they had no means of reaching hospital, then they would use the leaves of the nimm tree to make a tonic in the hope that this might help. But now, most of the villagers know how to manage malaria effectively.”

Centre for Innovation Against Malaria: during the rainy season in some African countries it’s not unusual for hospitals to be so inundated with young malaria victims that four children have to share one bed.

With up to two million malaria deaths a year — most of them in sub-Saharan Africa — it’s clear that the many initiatives to prevent the disease remaining one of the world’s major killers are not working. Despite advanced drugs, considerable progress with vaccine development and initiatives such as insecticide-impregnated bed nets, malaria continues to blight the lives of many families in Africa.
New approaches to tackling the problem are urgently needed, which is why the Centre for Innovation Against Malaria (CIAM) has been set up in The Gambia in association with the MRC, the National Malaria Control Programme and TESITO (a UK-based NGO). The CIAM aims to combat the disease by using a community-centred approach. It believes that for researchers to move from demonstrating the effectiveness of malaria interventions to seeing new health policy implemented, the community must understand and take responsibility for its part in the process. This means that consultation with the community and individuals is needed before they can be equipped to take action to help manage malaria.

**Life-saving bednets:** bednets treated with safe biodegradable pyrethroid insecticides protect people from malaria by reducing their exposure to malaria-infected mosquito bites. The MRC Laboratories, The Gambia, first demonstrated this in 1986, and in another study three years later showed that use of insecticide-treated bednets resulted in a 63 per cent reduction in deaths from all causes of children under five years.

Additional large-scale trials in northern Ghana, coastal Kenya and The Gambia showed that the nets saved children’s lives in other settings too. This prompted the UN/World Bank/WHO Tropical Diseases Research (TDR) Programme to fund research to improve methods for treating nets with insecticide. TDR also stimulated the private sector to develop and innovate, which has led to ‘dip-it-yourself’ kits, more durable nets and nets that do not need re-dipping. Since 1998, insecticide-treated nets have been used in the Global Malaria Programme (formerly Roll Back Malaria) with great success. But use varies from country to country – currently fewer than one per cent of people use the nets in Nigeria, whereas 76 per cent do in rural Gambia. The Global Malaria Programme’s goal is for 80 per cent of people in Africa at risk of malaria to be using them by 2010.

**A breakthrough in malaria vaccine:** the parasite that inflicts malaria has a remarkable ability to change its biological make-up, almost at will. This has made developing a lasting effective treatment an extremely difficult task. Despite much excellent research worldwide, the development of a vaccine has remained beyond the reach of medical scientists. However, the quest might be nearing its end. Recently our Laboratories in The Gambia have been the scene of extensive studies into what is currently the most promising malaria vaccine around, RTS,S/AS02A, developed jointly by Professor Adrian Hill of the University of Oxford, the MRC and GlaxoSmithKline.

Phase II clinical trials have shown that this vaccine can give 18 months’ protection to children, who are in the most susceptible group. Further, large-scale studies are being planned in Africa. And the results of such trials, which are carried out under the MRC/DFID concordat, often lead to valuable complementary studies in developing countries where there is currently no direct UK research activity.

**Tuberculosis (TB)**

**Change in WHO guidelines for TB treatment:** following a study carried out in 2004 by Professor Andrew Nunn of the MRC Clinical Trials Unit, the WHO changed its guidelines regarding the treatment of TB in the developing world. Professor Nunn showed that a six-month combination therapy regimen involving rifampicin was more effective than the WHO-recommended eight-month combination regimen of ethambutol.

**Respiratory infection**

**Translating research into national strategy:** the respiratory disease *Haemophilus influenzae* B (Hib) has almost been eradicated in the developed world. However, a lack of reliable vaccine supplies means it persists in Africa, where it is one of the most common causes of fatal meningitis and bacterial pneumonia in children. But following trials carried out by Professor Richard Adegbola, head of the bacterial diseases group at the MRC Laboratories in The Gambia, the country’s vaccination rate has reached 80 per cent and the disease has been almost eliminated among children. Professor Adegbola undertook two trials, one of which lasted five years, involving *Haemophilus influenzae* and *Streptococcus pneumoniae*. They showed that routine vaccination can eliminate Hib from a population despite health infrastructure problems in the country.

The success of this vaccination research is largely due to the involvement of the Gambian government and its willingness to make Hib vaccination part of the Gambian Expanded Programme for Immunisation. The government is now negotiating with the Global Alliance for Vaccines and Immunisation (GAVI) to secure funding for the programme beyond 2006. “But it is unlikely that the funding will cease because the results of the programme so far are so impressive,” says Professor Adegbola.

The GAVI is now interested in developing an evidence base to support the development of a Hib healthcare programme across those African countries where many
children are in danger of infection. This includes developing any existing immunisation programmes if the countries’ governments can be convinced of the need to do so.

**Vaccination against pneumococcal disease:** the Gambian government is now considering introducing national vaccination against pneumococcal disease following a four-year MRC study led by Professor Felicity Cutts, involving 17,000 Gambian children. The results showed that vaccination prevented infection caused by nine strains of pneumococcal bacteria in 77 per cent of children, leading to 37 per cent fewer cases of pneumonia. Overall, deaths among the children were reduced by 16 per cent. In addition, the vaccination programme reduced hospital admissions by 15 per cent – a result which has important implications for the limited healthcare resources of the developing world.

**Hepatitis B**

**Vaccination to pre-empt liver cancer:** as a result of a five-year trial by the MRC, every newborn Gambian child is vaccinated against hepatitis B. In The Gambia this disease is the most frequent cause of liver cancer, which in turn is the most common cancer among men and the second most common among women. The problem is seen throughout Africa, where unborn babies contract the infection from their mothers in the womb and then often go on to develop liver cancer as adults.

The MRC became aware of the high number of cases of hepatitis B in The Gambia in the 1970s. When in 1980 Professor Hilton Whittle found that prevalence was still high, he introduced a vaccination programme in villages in the Kiang region. The infection rate has been dropping ever since.

On the back of this success, Professor Whittle initiated a randomised control trial into the long-term effects of hepatitis B vaccination.

“This trial has become the longest-running, largest randomised control trial investigating vaccination against liver cancer anywhere in the world. It shows the real strength of MRC investment in research abroad. These results have convinced the Gambian government that it is worth investing in a vaccination programme and consequently they now make sure that every newborn baby is vaccinated against hepatitis B,” he said.

Professor Whittle’s research has influenced vaccination policy in Zimbabwe, Tanzania, Kenya and South Africa, with developing countries in Asia also following suit.

**Protecting the health of mothers and babies**

Of the 25 million underweight babies born every year around the world, nine out of ten live in Africa. These babies weigh less than 2500 grams at birth – the WHO definition of low birth rate – compared to an international average of around 3000 grams. If they are to develop properly and lead healthy lives, good nutrition is vital, but this can be hampered by the seasonal availability of food. Exposure to infectious diseases and inadequate care also have an impact. Together, these factors will often make a child particularly susceptible to infection and prevent their immune system from developing fully.

**Compensating for the ‘hungry season’:** MRC Keneba in The Gambia treats mothers and babies suffering from malnutrition. Research there led by Professor Andrew Prentice has shown that retarded growth in the womb is often caused by under-nutrition and that it predominates towards the end of the ‘hungry season’ between August to December, when there is less food available. In addition, the pregnant mothers who continue with heavy farm work after contracting infections are more likely to give birth prematurely. These premature births peak during July when farm labour is most intensive and in October when malaria infection is at its height.

By supplying at-risk mothers with dietary supplements, MRC Keneba has been able to reduce the incidence of retarded development in unborn babies and there has been a substantial reduction in stillbirths and early neonatal deaths. The Gambia now gives this intervention to pregnant women through its primary healthcare systems. Furthermore, such MRC studies with mothers and children have led the Gambian government to set up its own nutrition council to develop policy and strategy in this important area.
**Changing thinking about nutrition and health**

The breadth and depth of our Gambian research into the links between diet, maternal health and reproductive outcomes is unprecedented in other centres in low-income countries.

Here are examples of how the programme has had a significant influence on international policy and practice:

MRC research based on more than 5,000 pregnancies in rural Gambia has contributed to the new WHO strategy on low birth weight published in 2006. The results showed that the factors which cause low birth weight are different from those that cause babies to be born prematurely, which pinspoints the need for different measures to prevent the two conditions. The studies also showed that a mother’s ability to breastfeed her baby is highly resilient. Even when her nutrition is poor, lactation can be relied upon as the baby’s only food for up to six months. This has major benefits for infants, whereas early introduction of weaning foods inhibits the mother’s milk production and does not enhance infant growth. These findings contributed to the WHO’s consultation on the Optimal Duration of Exclusive Breastfeeding (2001) and the subsequent Global Strategy for Infant and Young Child Feeding (2002) that has now been adopted as policy in the majority of low-income nations.

MRC researchers have conducted in-depth studies on people’s more general nutrient requirements in The Gambia over many years. These have had a major impact on international dietary guidelines and on the recommended food levels in the reports *Human Vitamin and Mineral Requirements* (2002) and *Human Energy Requirements* (2004) by the WHO and the UN Food and Agricultural Organization. MRC work on calcium and bone health has been particularly influential in showing how people who do not consume much dairy produce can adapt to having very low calcium intakes.
Improving health, improving lives

Thanking our partners in the journey

In this booklet our aim has been to bring you a brief overview of the work of our African and UK scientists in the fight for better health for Africa. You will also have learnt about the vital contribution made every day by African people – communities, patients, MRC staff and governments. Their commitment and dedication is crucial. Without it, we could not hope to achieve our scientific goals.

Increasingly, our scientists in Africa achieve what cannot be done from the UK. They can build local and national commitment, develop regional networks, help to ensure that the outcomes of MRC research are translated into healthcare policy and practice, and shape the research agenda to match Africa’s changing health challenges. The MRC in the UK is proud to be a partner in this important and exciting journey.

We wish that there was sufficient space in Improving health, improving lives to include all the MRC-funded research that feeds into our work for Africa. For example, the world-class research into malaria, TB, HIV/AIDS and health behaviour that is being carried out in universities and MRC units and institutes in the UK. Collectively, this work forms a vital scientific powerhouse for generating new knowledge and methodologies. These findings are then translated into benefits for human health through applied research in Africa and the commitment of a range of partners – governments, NGOs and public-private partnerships.

As you will have read, our research for Africa dates back nearly 100 years – long before the continent’s health challenges became the focus of international media attention. The MRC will maintain and build on this long-term commitment, until we achieve our goal of healthier, more productive lives for everyone in Africa.

This page: Dr. Ogochukwu Ofordile checks the health of a child at MRC Keneba, The Gambia.