Malaria Advocacy -The Beginnings

1992-1995 Malaria Awareness Campaign

1995 Launch of MALARIA.ORG

1996-1997 Creation of Global Awareness through Conferences held in India.

August 1997 Malaria Fact Pack

May 1998 Launch of Roll Back Malaria

1999-2000 Drive Against Malaria

1999-2001 DTT Campaign

Current Perspectives 2005 - 2007

1992-1995

Malaria Awareness Campaign

With the backing of its 25-member inaugural Scientific Advisory Board comprised of leading malaria scientists from around the world, the MFI created initial attention for the need of global efforts to fight malaria.

1995

Launch of MALARIA.ORG

In 1995, the MFI launched the first comprehensive *www.malaria.org* website to bring together information about malaria. This website has been a gateway for malaria-related information and has facilitated other efforts to fight malaria. In 1995, the development of the internet and websites were in their infancy with information on malaria not readily available, and the information posted was the product of MFI's Advisory Board and volunteers.

The initial MFI website was constructed with the support of Brad Landers of Net Node, Inc. The MFI acknowledges the foresight of former Board member Dr. Robert H. Nagel for securing the malaria.org domain. In 1996 the MFI established the first online dialog system for discussions on malaria. From 1998 through 2005, the site was developed and maintained by Dr. Kathryn Nason-Burchenal as vice-president of communications for the MFI. In 2006, the MFI website was reconstructed with the technical leadership of Sudeep Rangi and colleagues from Emory University's Student Coalition Empowering Emerging Nations (SCEEN) and staff volunteers from Emory's International Center for Malaria Research and Education (ICMRE).

1996-1997

Creation of Global Awareness through Conferences held in India.

MFI organized an International Symposium on Malaria in New Delhi, India, in 1996 at the annual Meeting of the Indian Society of parasitology. The Ronald Ross Centenary Conference (pdf) in August 1997 was a direct outcome of the success of this symposium. invited speakers from the 1996 Symposium played instrumental roles in the organization of the 1997 event. Over 800 people attended This landmark conference, and the creation of global awareness was achieved for the first time.

August 1997

Malaria Fact Pack

In support of the Ronald Ross Centenary Conference, the MFI developed the first malaria awareness press kit including the Malaria Fact Pack (pdf) to help attract widespread global media attention on malaria. The Malaria Fact Pack was developed with contributions and extensive review from over 30 international experts from the MFI Scientific Advisory Board and professional network. This historical document became the framework for the development of various future malaria advocacy documents produced by MFI and others.

May 1998

Launch of Roll Back Malaria

MFI's success bringing attention to the world about malaria in 1997, led to the realization that it was possible to get the media's attention and that there was a global interest in this deadly disease. This realization led to intensive brainstorming sessions that resulted in the creation of Roll Back Malaria. The original flyer (pdf) produced to launch the Roll Back Malaria initiative was developed by the UK Department for International Development and the MFI (please disregard the 1998 outdated contact information on this flyer for the MFI and DFID). To accompany this flyer, MFI produced a Malaria Background Information (pdf) document. The launch of RBM occurred in May 1998 at the time of the G8 Summit in Birmingham, UK, and the arrival of Dr. Gro Harlem Brundtland as the new director of the World Health Organization.

1999-2000

Drive Against Malaria

Along with MEMISA, the MFI was instrumental in launching the Drive Against Malaria Campaign led by David Robertson, an adventurer from the UK. In 1999, MFI arranged for Robertson and his Land Rover to be featured in the exhibit hall, at the Second Multilateral Initiative on Malaria (MIM) meeting, in Durban, South Africa. This began the relationship of David Robertson with hundreds of scientists from Africa and around the world. Immediately after this meeting, with MFI's management and Louis Da Gama as the project director, David Robertson began his major expedition to create awareness in Africa among political leaders and the media. Departing from South Africa, David began this historic journey transversing Africa delivering information about this deadly disease. The MFI remains supportive of David Robertson's continued efforts to fight malaria.

1999-2001

DTT Campaign

In 1999 the United Nations Environment Program began negotiating a treat to eliminate the use of 12 persistent organic pollutants (POPs), including DDT. Over 300 environmental groups, such as Greenpeace, World Wildlife Fund, and Physicians for Social Responsibility, advocated a total DDT ban to be effective as early as 2007. The Malaria Foundation International (MFI) and the Malaria Project (MP), led by Dr. Amir Attaran, initiated a campaign to make sure that DDT was still available for use in malaria vector control. DDT remains the most effective and least expensive method for preventing the transmission of malaria in many regions of the world. MFI and MP garnered the support of over 400 doctors and scientists from 63 countries during their campaign (See original letter. The campaign against the total ban of DDT ended as a success. The treaty (pdf) approved by UNEP in 2000 called for the complete elimination of eleven POPs, with the twelfth POP, DDT, to be limited to restricted use in disease vector control. Read the original Open Letter and the list of signatories. .Additional information about the DDT Campaign is available in the MFI archives & ongoingly since 2000 with the leadership of Africa Fighting Malaria and leaders behind the Kill Malaria Mosquitoes Now (KMMN) campaign. See www.fightingmalaria.org for regular updates, educational materials and advocacy opportunities.

2004

Artemisinin-based Combination Therapy

The MFI was one of the organizations that took a stand in 2004 to support a major global switch to the use of Artemisinin-based Combination Therapies. At this time, cheep but largely ineffective malaria drugs were being used, while the more expensive ACTs were underfunded and underutilized. This scenario has changed dramatically with the publication of an article in The Lancet titled "WHO, the Global Fund, and medical malpractice in malaria treatment "(pdf). Since, the Global Fund, WHO and many others have been focused on funding and delivering ACTs as an important effective therapy to fight malaria.

Current Perspectives: 2005-2007

Read the Global Vision Magazine Article (Pages 1 and 2, pdf) featuring the MFI's 2005 Hedge Funds vs Malaria Leadership Business Conference.

View - Rallying the World Against Malaria

Back to About MFI

Malaria Foundation

Global Networks Against Malaria

www.malaria.org

Malaria Awareness Campaign (MAC)

- MAC Projects a s
- How can I get MALARIA? (see Malaria Life Cycles)
- Guides for Travelers
- News Articles on MALARIA
- Other MALARIA Resources
- Listserv: Open Forum on MALARIA

MALARIA is a Major Ongoing Disaster.

- **The numbers are staggering!**
- **Half of the world's population - 2.5 billion people - lives at risk of getting MALARIA.**
- **Three hundred million to 500 million people become sick with this disease each year.**
- **MALARIA kills several million people each year, and a few hundred each hour.**

- **Each minute, 3 to 5 children die of MALARIA!**
- **Each year, MALARIA is believed to kill nearly as many people as AIDS has killed in the past 15 years (~3 to 4 million).**
- **Each year, MALARIA kills up to six times as many people as were killed in the 1994 Rwanda massacres (~500,000).**

- **Each hour, MALARIA kills more people than did the 1995 EBOLA epidemic in Zaire (~250).**
- **However, MALARIA is not recognized in the developed world as a disaster like AIDS, EBOLA, or the Rwanda massacres.**
- **These are tragedies, but so is MALARIA.**
- **MALARIA has not been a high-profile disease; exotic viruses or disasters that kill rapidly tend to make the Front Page.**
- **People with serious cases of MALARIA lie in comas; they enter a profound sleep, far from any cameras.**

Global Awareness

MALARIA is a global problem, in need of concerted efforts at a global scale!

The Malaria Foundation is committed to informing the world about MALARIA, the scope of the problem, and how it significantly affects social well-being, economic growth, and development worldwide.

Malaria is a serious problem in about 100 countries! This is a major reason for concern!

MALARIA is NOT only a problem of tropical countries!

Over the past 10 years, the geographical distribution of MALARIA has been increasing to Northern areas. There has been reinvasion of MALARIA for example in areas of northern India, Turkey, and Russia, as well as occasional small outbreaks in Europe and the United States; see review of recent outbreaks in the U.S. In fact, two malaria cases were just identified (August 1996) that were transmitted in Palm Beach, Florida, USA. (see other on-line reports....)

MALARIA transmission is possible if the weather conditions are right to support the growth and infection of Anopheline mosquitoes and if a “reservoir” of MALARIA parasites is available. Anopheline mosquitoes exist in many Northern areas, including the United States and Europe. The MALARIA parasite reservoir becomes available in non-malarious regions when people - travelers or immigrants - arrive from MALARIA endemic countries with MALARIA. As more people travel to and from MALARIA endemic countries, the probability of having MALARIA transmission in non-endemic areas increases.

MALARIA transmission can occur if an Anopheline mosquito becomes infected by biting a person with

MALARIA, and then later bites an uninfected person (see Malaria Life Cycles). MALARIA transmission in developed countries has also been traced directly to airplanes or ships carrying infected "stow away" Anopheline mosquitoes.

MALARIA: Drug Resistance.

The spread of drug resistant MALARIA is one of the greater reasons for concern about MALARIA worldwide.

No one is fully protected from getting MALARIA, even if he or she is taking prescribed drugs to prevent this disease. The MALARIA parasite has developed resistance to all of the commonly used anti-malaria drugs. This means that there is no guarantee that these drugs will be effective in preventing or curing a given infection. Today's commonly prescribed drugs also have known side-effects, which can differ from person to person.

People from the developed, non-malarious world should be especially aware of the dangers of MALARIA if they, their friends, or family members plan to travel to these malaria-endemic countries. And all doctors should be aware of MALARIA and be trained to consider and recognize it as a possible diagnosis.

Lack of physician awareness has led to misdiagnoses in developed countries. This can be deadly! The most serious type of MALARIA (*Plasmodium falciparum*) can kill within a few days if not treated. This is a major threat to travelers in endemic areas, whether tourists, short-term employees, journalists, military personnel, refugees, or government officials; tourists alone comprise over 20 million people annually.

For additional information, please refer to other malaria resources. Be aware that individual sources differ in their recommendations for prevention or treatment! It is WISE to consult a knowledgeable physician before traveling to places where there is MALARIA.

Additional research on MALARIA prevention and treatment is urgently needed. Malaria drug resistance has been steadily increasing for a few decades, and its cause is not fully understood. New effective and safe compounds and/or drug regimens to prevent and treat MALARIA must be identified, developed, and applied.

MALARIA: Global Education.

Many people in industrialized countries incorrectly believe that MALARIA has been eradicated, or that it is a minor problem; some only recall MALARIA as a health problem of colonial times, or as a health problem encountered by military personnel; for example, from the World Wars or the Korean or Vietnam Wars; others are aware that it affected soldiers in Somalia, or that Mother Teresa was stricken twice with MALARIA.

Few realize the real impact of this disease. Most are astounded to learn the truth about MALARIA. As people begin to learn the seriousness of this problem, they have been drawn to help. The response of the public has inspired the MALARIA FOUNDATION's slogan "***Global Networks Against Malaria***" and its program, "Networks Against Malaria."

Tackling MALARIA will require the participation, cooperation, networking, and teamwork of people worldwide.

It is crucial that the media and politicians are well informed and encouraged to support MALARIA Education Campaigns. Continued forceful efforts must be made to ensure that the seriousness of the present MALARIA situation in the world is conveyed, especially to those responsible for making decisions about the allocation of public funding for health research and health care. The public should also be informed and given the opportunity to contribute financial or voluntary support.

Remember the focus of the problem! The MALARIA FOUNDATION recognizes the potential threat that MALARIA poses to the people of developed countries and encourages people to learn about this disease and take precautions when traveling to malarious regions of the world. However, MALARIA especially affects the people living in developing countries. We strongly emphasize the global nature of this problem and are creating opportunities for people to band together and join in the fight against MALARIA worldwide.

MALARIA: The Global Economy.

MALARIA limits international trade and development.

The ultimate tragedy is that the part of the world that is continuously at high risk of contracting MALARIA is predominantly the poorest half. However, in today's global marketplace, with expanding industrial activity in the MALARIA endemic half of the world, this disease must be recognized as a serious stumbling block for widespread international trade and development.

MALARIA impedes the growth and development of international companies, as well as the development of national companies in these areas who could be the consumers of international products. In fact, the direct annual economic losses due to MALARIA in Africa alone amount to 1.8 billion U.S. dollars.

In several cases, recent outbreaks have been noted in places where MALARIA had previously not existed or had been under control. Moreover, there are now several of these instances where malaria is spreading from the countryside into city limits, creating an unsafe environment for city dwellers and visitors, including businessmen and tourists, to these cities. In some areas, such as in India and Eastern Europe, there has been a rise in the most severe and deadly type of MALARIA, *Plasmodium falciparum*. Other countries such as Brazil and Thailand are experiencing greater MALARIA of different types due to deforestation or mining activities. Environmental, economic, and political issues are often very clearly intertwined with the increase of MALARIA.

The MALARIA problem is also the direct result of a lack of adequate prevention and control measures. A MALARIA vaccine does not yet exist and malaria parasites resistant to all commonly available drugs are now prevailing. Also, World Health Organization (WHO) control programs of the 50's and 60's, which were aimed at eliminating mosquitoes with the extensive use of insecticides, have proved to be largely

ineffective. Most notably, mosquitoes have become resistant to DDT, and have learned to avoid it as well. Eradicating MALARIA-carrying mosquitoes, on a global scale, proved to be unrealistic.

Meanwhile, mosquito netting, if available and used properly, can provide some protection. And research is underway to develop malaria vaccines and drugs. Contrary to what many might think, there is a tremendous market for new agents against malaria! Support to help discover and effectively apply antimalarial tools, ultimately, will be invaluable for the recipients and profitable for the providers!

There are also many opportunities to link health improvements with development and in the process improve national and global economies. The current malaria situation partly stems from the preponderance of poor health care systems and the frequent lack of a strong political will and commitment to improve health services. Moreover, educational programs and other community initiatives to help stop the spread of MALARIA are limited or non-existent. Development programs can help to decrease malaria!

- MALARIA prevents economic growth but can also result directly from the lack of development.
- (see Other resources, including book lists & recent news articles for more information.

MALARIA: Global Participation.

Networking, Communication, Research, and Malaria Control

There are no easy solutions to halting the spread of MALARIA!

However, effective networking and collaboration worldwide are essential. It is crucial to strengthen and maintain expertise in the field of MALARIA and to draw upon experts in other disciplines as well. Much has been learned since researchers first discovered the malaria parasite, and that it is transmitted by mosquitoes (~100 years ago). As we enter the 21st Century, it is an important and necessary time to evaluate the directions that have been taken to harness this problem, to learn from these directions, and to develop new global strategies. It is becoming apparent that these strategies will include greater networking and coordination of efforts worldwide, and that this will largely be facilitated by the communication potential of the Internet. The Malaria Research Network and World Wide Malaria Directory are two novel interactive database mechanisms/resources that are being developed on the web as steps towards optimizing communication and worldwide productivity in the areas of MALARIA research and control.
There is an urgent need for greater resources.

Despite the enormity of the MALARIA problem worldwide, there is limited financial support available from traditional sources for MALARIA research programs - ***only*** about 25 U.S. cents is spent each year worldwide per person sick with MALARIA!

Malaria Foundation

Global Networks Against Malaria

www.malaria.org

Our Mission is to facilitate the development and implementation of solutions to the health, economic and social problems caused by malaria.

Each year, 300-500 million people become ill with malaria and several million die.
Most who die are children under five.
200-300 children die from malaria each hour.
Pregnant women and non-immune adults are also severely affected.
Families and communities suffer worldwide,
as do national and global economies.

About the Malaria Foundation	Malaria Research Network
Resources on the Web.... General resources related to malaria	World Wide Malaria Directory
"Second Global Meet" - ***Main Page:*** Everything you need to know..... Travel Scholarships The Speakers..... The Sponsors..... Audio on the Internet "First Global Meet" Photographs	For the Scientific Community Links to numerous scientific resources • Malaria Genome Focus Group Working Document: Please send your comments ASAP & request copy of the Final Document.... Your feedback is crucial!
Malaria Awareness Campaign	Network Against Malaria

20th August 1897

▼

Sir Ronald Ross
one of the most distinguished and creative
individuals
in the history of tropical medicine, on this day,
in **Secunderabad, India**, first revealed the
nplex development of malarial parasite in the mosquito,
ne of the most dramatic discoveries in medical science

20th August 1997

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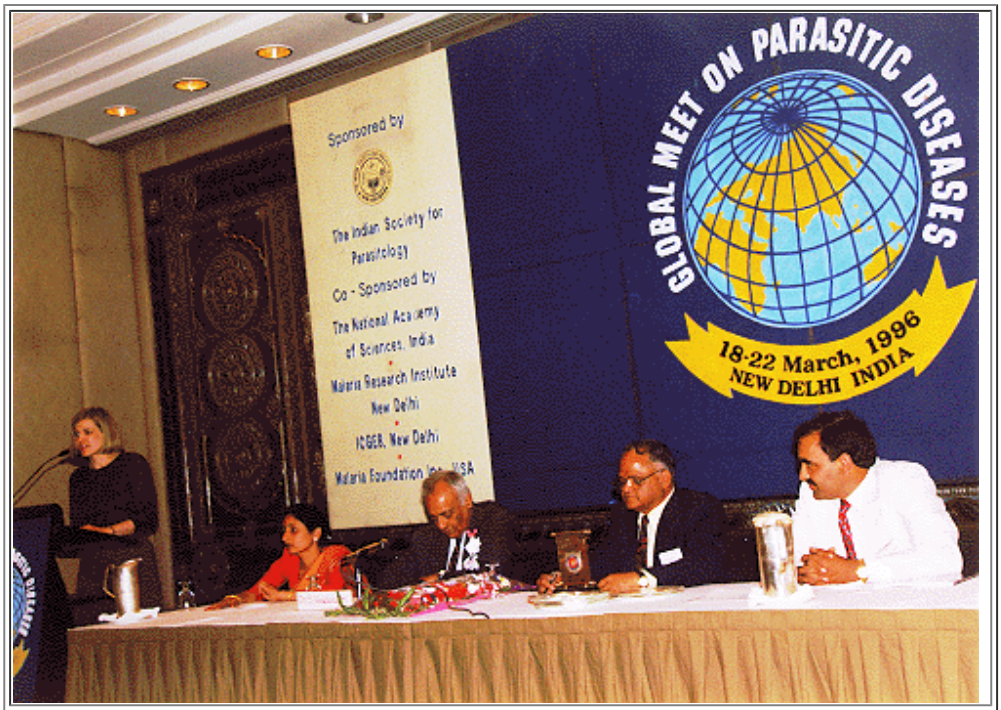
On the centennial of this discovery, you are
invited to attend the

Second Global Meet on Parasitic Diseases
with a focus on Malaria

18 - 22 August, 1997 • Hyderabad • India

SECOND GLOBEL MEET ON PARASITIC DISEASES
18 - 22 August, 1997
HYDERABAD • INDIA



This information was gathered in 1997 by the Malaria Foundation International with contributions from over 30 international experts.

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1. Scale

- Around 2.5 billion people (at least 40% of the world's population) are at risk in over 90 countries.

- Malaria causes or contributes to 3 million deaths and up to 500 million acute clinical cases each year. In other words:

- Almost as many deaths per annum as the AIDS death total in the last 15 years

- 20 times more deaths each day than deaths from the 1995 EBOLA epidemic in Zaire (~250).

- Cause of more military casualties than bullets in every 20th century war in malarious regions

- The majority of deaths are children. In other words, children are dying at a rate of 4 per minute, 5,000 a day and 35,000 a week.

- Other high-risk groups include pregnant women, refugees, migrant workers, and non-immune travelers - over 20 million Western tourists at risk annually.

- The main areas affected are Africa, South East Asia, India and South America but surveillance and records are too poor to know the real distribution and case numbers.

- Malaria is one of leading causes of morbidity and mortality in the developing world (along with TB, acute respiratory syndrome, diarrhoea and HIV) but still not recognised in developed countries as a disaster like AIDS or EBOLA.

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2. Spread

Malaria kills more people today than three decades ago. Reasons for the spread include:

- Increasing drug resistance
- Increased migration and immigration
- Increase in size of endemic territories (e.g. people moving from countryside to cities)
- Tourist and business travel (increased air travel since 1950s/60s)
- Decreased mosquito control efforts (insecticide spraying)
- Deforestation and mining (development activities)
- WHO predicts an extra 80 million cases of malaria annually by the end of the 20th Century -i.e. a 16% increase within 3 years.
- Malaria is spreading to new territories for example, India, Brazil, Sri Lanka, Turkey, and the Middle East.
- Malaria is spreading from the countryside into cities (e.g. Bombay/Mumbai), increasing the risk for city dwellers and tourists in these 'safe' zones of endemic countries.
- International travel is increasing and travelers are increasingly at risk, especially given the difficulty in ensuring proper prevention by systematic drug intake.
- Climatic conditions and increased immigration mean that malaria could spread to the West (e.g. Florida) within 10 years. There have been recent reported cases in Florida, New Jersey, California, Georgia, Michigan, New York, and Texas. Historical precedents for Northern malaria include:
- US - endemic from colonial times to early 20th century
- Cases as far north as Siberia and Canada up to the 1950s
- Paris epidemic in the 1940s due to local mosquitoes infected via troops from Africa
- Widespread indigenous cases around the Mediterranean up to the 1960s
- 30 years ago, malaria had been eradicated or dramatically reduced in 37 countries (WHO insecticide spraying programme 1956-69) but this situation has been rapidly reversing, especially over the last decade. The reversal is largely due to the cost of sustaining programmes, loss of motivation in the face of a seemingly declining threat, and the development of insecticide and drug resistance.
- India's malaria eradication programme in the 1950/60s reduced infections from 75 million to 100,000 per annum and fatalities from 800,000 to almost none. Over the past two decades, the trend has reversed with four major epidemics since 1994. In 1996, 2.85 million cases were reported, and the official - and under-reported - death toll was around 3,000.
- In 1960 malaria was practically eradicated in Azerbaijan but by 1995 reported cases reached almost 3,000 across two-thirds of the country. The main cause is the recent influx of refugees into the endemic South.

- *Plasmodium vivax*, the classically 'benign' malaria (which has been known to make people very sick but not kill them), is now believed by some experts to be potentially lethal in cases involving drug resistant parasites. In 1994, *P.vivax* was reported resistant to chloroquine in several Indian cities and districts.

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3. Cost

- Malaria exacts an enormous toll in lives, medical costs and days of labour lost. Educational systems also suffer as large numbers of children miss several weeks of school each year in endemic regions.

- The direct annual commercial loss in Africa due to malaria is currently estimated to be US $1.8 billion a year. In 1987 the figure stood at US $800 million. If this trend continues, the cost is likely to reach US $3.6 billion by 2000 (US $10 million a day).

- A single bout of malaria is estimated to cost a sum equivalent to 10-20 working days in India and Africa.

- India will spend US $40 million on malaria control in 1997 - up 60 per cent from last year. It is also planning a five year programme targeting 210 million people in 100 high risk districts that account for 80 per cent of all potentially fatal cases in India. This US $215 million programme will be funded primarily by a World Bank loan.

- The average cost of current treatment per dose ranges from US $0.08 and US $10.00 depending on the type of drug.

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4. Obstacles to Remedial Action

Political commitment

- Insufficient political commitment for improved health services

- Inadequate surveillance and control programmes

- Insufficient international public funding

- Inadequate training/career opportunities for local malaria scientists/health professionals

Resistance

- Drug resistance is increasing rapidly, largely due to widespread uncontrolled and unregulated drug distribution.

- Drugs have been used until resistance has rendered them ineffective, after which closely related drugs that are introduced show reduced efficacy and severely compromised life spans.

- Today, there are few effective anti-malarial drugs - most tropical countries still rely on chloroquine (which is increasingly ineffective) primarily due to cost and the limitation of alternatives.

- The vicious circle of new drug resistance limits research and rollout options and increases the cost of R&D - it is hard to establish whether to use new options widely, risking resistance, or keep them in reserve until resistance to existing drugs such as chloroquine or quinine becomes widespread.

- Another underlying factor contributing to the development of resistance is the improper usage of the drugs; for example, subcurative doses - people feel better, so stop taking their medicine, and some resistant parasites may be given the chance to survive and be transmitted by mosquitoes.

- There is insufficient research into novel drug targets. Current new options are based on the same three families of compounds (the quinolines, antifolates, and artemesinin derivatives) all of which have records of resistance and/or ineffectiveness.

- Insecticide programmes have also been hampered by the emergence of resistance to DDT and other insecticides.

Vaccine development problems

- Parasites have a more complex structure than viruses and bacteria and change appearance over the course of an infection. Finding the best way to attack them via vaccination is not easy - further research on their composition and biology is needed even before addressing major issues such as how to produce and administer a vaccine.

- The two main malaria parasite species are sufficiently different from each other that a vaccine based on one will probably not prevent malaria by the other.

Gaps in essential research

- Biochemistry of the parasite

- Basis of parasite drug resistance

- How people build up immunity to malaria

- Transmission characteristics and epidemiology (differs throughout the world)

- Pathogenesis (i.e. development characteristics of malaria)

- Mosquito biology, infection, genetics, insecticide resistance

- Effect of malaria on other diseases and vice versa

- Environmental factors

Inadequate international co-ordination of research efforts

Some progress has been made over the last decade but there is still a growing need for multi-lateral initiatives to co-ordinate research, training, and control efforts. Recent actions include:

1991 - "Malaria: Obstacles and Opportunities" published; A report of the Committee for the Study on Malaria Prevention and Control: Status Review and Alternative Strategies Division of International Health; Institute of Medicine, USA. Important committee recommendations put forward.

1992 - Ministerial Conference on Malaria in Amsterdam (WHO and Dutch sponsored): Ministers of health adopted a Global Malaria Control Strategy. The World Health Assembly, The Economic and Social Council of the UN General Assembly and the United Nations (UN) General Assembly subsequently endorsed the Strategy. Its goals are to promote early diagnosis and treatment, ward off epidemics and engage communities in mosquito control programmes. This has led to Action Plans in a number of African countries and, more recently, the Harare Declaration (see below).

1992 – Founding of the Malaria Foundation International (MFI)

1993 - Regional Task Force for Malaria Control in Africa (Established by WHO/AFRO with US AID [Agency for International Development] Support)

1996 - Malaria Research Worldwide; An Audit of International Activity (Wellcome Trust sponsored audit; publication available): Determination that only $ US 84 million is spent annually on malaria worldwide. This is extremely low considering the scope of this problem and the number of people, families, and communities severely affected.

1997 - "The Year for Malaria": major turnaround in outlook for this disease; strong renewed interest; optimism for continued momentum and scientific breakthrough.

January 1997 - International Conference on Malaria: Challenges and Opportunities for Collaboration in Africa; Dakar, Senegal: Groundwork laid for Multilateral Initiative on Malaria (MIM), which became official in July, and an appeal to the international community to mobilise in the fight against malaria (Nature, Vol 386, page 541)

February 1997 - A Meeting of Experts on Malaria Control Initiative in Africa; Brazzaville, Congo: WHO/AFRO meeting to develop initiatives to accelerate the implementation of malaria control in Africa.

June 1997 - Harare Declaration on Malaria Prevention and Control in the Context of African Economic Recovery and Development (by the Heads of State and Government of the Organisation of African Unity); Harare, Zimbabwe: Proposed plan of action and budgetary needs published.

June 1997 - Malaria Genome Consortium meeting; Cambridge; England: Progress and increased commitment to malaria DNA sequencing and analysis efforts demonstrated by the leading funders and scientists involved in this research.

July 1997 - Multilateral Initiative on Malaria (MIM; The Hague, The Netherlands: a strong coalition of several of the world's major research agencies, medical charities and donor agencies, which have joined forces to explore ways forward in the fight against malaria. Began in Dakar, Senegal in January and officially took root in The Hague, The Netherlands in July. One immediate goal of the MIM is to greatly improve the global networking and research capabilities of scientists. The other major goal is to facilitate research developments (and hopefully breakthroughs) via new and regular multilateral partnerships and collaborations. A follow-up meeting will be held in England in six months' time.

August 1997 - The Ronald Ross Centenary Malaria Meeting (The Second Global Meet on Parasitic Diseases - with emphasis on malaria); Hyderabad, India; August 18-22, 1997. This meeting, in large orchestrated by the MFI, is a very strong demonstration of the commitment of scientists and public health officials to malaria research and control. Over 100 of the world's leading malaria scientists are scheduled to speak and over 650 people are registered to attend. Goals of the meeting include the strengthening of scientist co-operation aimed at reviving public and funding agencies interest in this forgotten disease.

5. Investment in Research

Global expenditure on research per associated death for various diseases

Diseases	Annual global research ($ million)	Global mortality (1990: Thousands)	Estimated global research expenditure per fatal case worldwide (1990)
HIV/Aids	952	290.8	3274
Malaria	**60**	**926.4**	**65**

- Limited national and international research budgets - US $84 million spent on malaria research in 1993 versus US $2.3 billion per annum for cancer, US $1.5 billion on AIDS, US $300 million on Alzheimer's.

- The USA is the largest single country contributor to malaria research (US $35 million in 1994) but its budgets have declined over the past decade. It is now increasing its support. The National Institute of Allergy and Infectious Diseases of the National Institute of Health (NIH/NIAID) is the leading sponsor.

- Europe as a block invests at least as much as the US. The European Commission has become one of the leading supporters of research in partnership with developing country scientists.

- Total malaria expenditure in the UK has been increasing over the past decade, from approximately US $4 million in 1985 to approximately US $15 million in 1994. The Wellcome Trust has been a major sponsor of malaria research, primarily in the UK and Africa.

- In Asia, the Thai government is leading a five-year US $12.5 million research programme (40% National Science & Technology Development Agency, 40% the Thailand Research Fund and 20% funding from the WHO's Tropical Disease Research Programme).

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6. Infection Basics

- There are four species of human malaria parasites but only two are highly prevalent: *Plasmodium falciparum* and *Plasmodium vivax*

- *P. falciparum,* the major cause of malaria deaths, accounts for around 90% of African malaria and about 50% in South East Asia/Latin America.

- *P. falciparum* may exist in blood at low non-clinical levels (due to partially effective immunity or incomplete drug treatment) and then increase to cause obvious illness.

- *P. vivax* can lie dormant in the liver and relapse up to several years after the initial illness. Cause of relapse "trigger" is unknown.

Carriers of Infection

- All human malaria is spread by female 'Anopheline' mosquitoes which need a supply of blood in order to produce and lay eggs.

- These mosquitoes become infected by taking blood from an infected individual.

- Malaria can also be transmitted by blood transfusion, contaminated needles and syringes, and in rare cases, from mother to child before and/or during birth.

How human malaria infections occur

- The malaria parasite reproduces inside the infected mosquito forming a sac with thousands of new malaria parasites. (Development of the parasite inside the mosquito is influenced by the outside temperature).

- In order to infect an individual, the infected mosquito has to live 15 days at which point the parasites burst out of their sac and reach the salivary glands of the mosquito.

- As a mosquito bites it injects infected saliva.

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7. Malaria cycle

There are three main stages:

Stage I: Upon infection by the mosquito, the malaria parasites move rapidly into the liver - within ~30 minutes - and reproduce there rapidly for 5 days or more, depending on the species (*P. falciparum* or *P. vivax)*.

Stage II: The malaria parasite breaks out from the liver, enters the bloodstream, and within minutes invades red blood cells, where they grow and divide. Every 48-72 hours (time differences depend on the species) the red blood cells rupture, dispersing more parasites along with waste products/toxins into the blood stream. This step causes fever, chills, and anaemia in the victim - telltale clinical signs of malaria. The released parasites then invade other red blood cells, beginning the cycle again.

If untreated, the malaria disease can progress causing a variety of serious complications. Most seriously, *P. falciparum* parasites cause blockage of blood vessels; cerebral malaria, coma and death can ensue. For sufferers without partial immunity (e.g. Western travelers, migrant workers), it is possible for death to occur in only 24 hours after the first appearance of symptoms.

P. vivax does not adhere to blood vessels and cause the associated complications; however, unlike *P. falicparum,* dormant *P. vivax* can burst out of the liver into the bloodstream months or several years later ready to start the vicious clinical cycle again.

Even if not fatal, malaria infection can potentially make a person vulnerable to death from other causes.

Stage III: Some parasites invade red blood cells and develop into sexual forms that are ingested by uninfected biting mosquitoes, within which they mate and begin to reproduce. These parasites make their way to the salivary glands of the mosquito, ready to move on to another victim when the mosquito takes its next blood meal.

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8. Treatments

- *Quinine,* a natural product from the bark of the Cinchona tree, was one of the first treatments for malaria and appeared in the 17th Century. It is still effective but can be toxic. *Quinine* remained the drug of choice for treatment and prevention until 1942 when chloroquine took over. With widespread chloroquine resistance, *quinine* together with artemether have become the two major and best available treatments today - for any type of malaria. In countries where quinine resistance is developing, it is used in combination with other therapies such as tetracyclines and clindamycin.

- *Chloroquine* was first used in the 1940s and is a weekly course. Today it is manufactured by all the major pharmaceutical companies. The first cases of resistance were found in South America and South East Asia in the early 60's and is now ineffective almost everywhere. However, it is still the widest used anti-malarial (mainly in Africa) as it is the cheapest drug available; in some countries, only less than US $0.10 per tablet.

- *Sulfadoxone/pyrimethamine (Fansidar SP)* was developed in the 1960s. The course comprises three doses taken together on one day. Today, this drug is manufactured by a number of pharmaceutical companies, although the *Fansidar* trademark belongs to Hoffman LaRoche. Despite widespread resistance in South East Asia and parts of South America, it is starting to become the first line of treatment in some African countries where chloroquine resistance has been widespread. Malawi and Kenya have made an official commitment to using Fansidar but others are reluctant to follow due to perceived increased cost and/or logistics problems encountered in trying to introduce change into their health systems. Generic SP may cost as little as US $0.11 per tablet.

- *Mefloquine (Lariam)* was developed by the US army in the early 1980s and commercialised by Hoffman LaRoche. Resistance has been observed since the early 1980s particularly on the Thai/Cambodia and Thai/Burmese borders (50% resistance). Some people have reported some side-effects such as dizziness and nausea.

- *Halofantrine* was also developed by the US army and marketed by SmithKline Beecham in the 1990s. Cross-resistance with mefloquine and side-effects (sometimes severe) have been observed. At US $ 10.00 the treatment is relatively expensive and impractical for public health use.

- *Artemisinins* (derived from ancient Chinese herbal remedy) comprise a family of products. The two compounds most widely used are artemether and artesunate, mainly in Southeast Asia but not widely used in the developed world in part due to toxicity fears, licensing and logistic issues. More research data is needed for these products to meet international standards. Due to the high rate of treatment failures, artemisinins are now being combined with mefloquine. As such, they are very effective. Artemisinins are manufactured by both the Chinese and Vietnamese State Manufacturing Units, as well as several companies.

- All the above are treatments for *P. falciparum* or *P. vivax* malaria cases. P*rimaquine* is the only treatment available for eliminating the dormant forms of *P. vivax* which remain in the liver. Resistance to primaquine has been noted in the past few years.

Future treatment possibilities

There is an urgent need for the development of new drugs based on new compounds. In the meantime, combination therapies based on current drugs are being tested which include:

Licensed

- *Azythromicine* - a doxycycline replacement for children and pregnant women.

- *Malarone* (Glaxo Wellcome*;* atovaquone/proguanil HCl*)* gained its first license in October 1996. Licenses are being sought worldwide. Clinical studies are ongoing.

- *Arteether* - License imminent

In later stages of clinical development

- *Co-Artemether* (Novartis; Benflumetol/Artemether*)*.

- New generation 8-aminoquinolines for curative treatment of *P.vivax*, possible replacement for primaquine (From India, CDRI 80/53, and from the US Army, WR238605)

Other

- Novel associations such as cycloguanil-dapsone (similar to what Fansidar is made of)

- *Pyronaridine* - evaluated in China and being reassessed by WHO but proven effective in limited treatment of African patients.

- Chloroquine analogues and combination therapies

Although, the above compounds are in different stages of testing and clinical trials, it is important to note that none have the promise, as well as the combination of ease of use, efficacy, and low cost that chloroquine had when it first came on the scene as a "wonder drug" in the 1940's.

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9. Preventatives

Drugs

- Prophylactic recommendations vary according to the preference of different countries and also individual doctors. The majority recommend Mefloquine (Lariam) for non-immune travelers, a weekly treatment. It is approximately 90% effective. However, some people have reported side effects**,** among them dizziness and nausea.

Vaccines

- No vaccine yet available for use. Increased R&D is needed for vaccine development.

- An experimental vaccine candidate against the infectious mosquito stages is currently undergoing Phase III Clinical trials led by SmithKline Beecham Biologicals (SBBIO).

- Additional peptide and DNA vaccine candidates are being tested in early Phase I clinical trials.

- Other potential vaccine candidates need to be explored further for each stage of the malaria infection.

Other

- Protection against mosquito bites using skin repellents, mosquito nets etc can help, when feasible.

- Addressing environmental, development and educational issues/perspectives can help to immediately reduce morbidity and mortality.

Insecticide Treated Bed Nets (ITBN)

- The WHO Tropical Disease Newsletter (Jan 1997) suggested that the lives of some 500,000 young African children might be saved every year from malaria if bednets, treated with biodegradable pyrethroid insecticide, were widely and properly used. Because they are treated with insecticide, they not only prevent mosquitoes from attacking victims but also kill the mosquitoes.

- A 1991 study in the Gambia (West Africa) showed a 63% reduction in childhood mortality using ITBNs. A second study in The Gambia revealed a 25% reduction in all-cause child mortality. More recently (1996) in Kilifi, Kenya, under very different epidemiological and cultural conditions deaths were cut by a third.

- However, it is possible that the initial reduction of mortality may not be sustainable. Longer term studies on ITBN effectiveness need to be undertaken.

- ITBNs are costly and uncomfortable in the hot and humid tropics so their practicality must also be evaluated. Alternatives such as insecticide impregnated curtains are also being considered.

Insecticide Treated Bed Nets (ITBN)

Country	**% reduction in all-cause child mortality**	**Project Organizer**
The Gambia	63	Medical Research Council Laboratories, The Gambia
The Gambia	25	Gambian National Bednet Impregnation Programme
Kenya	33	WHO organized trials
Ghana	17	WHO organized trials

10. Brief 100-year History on Anti-malarials

circa. 1880	Laveran discovers malaria parasite
20 August 1897	**Sir Ronald Ross reveals the complex development of the malarial parasite in the mosquito. Quinine was drug of choice at this time**
1932	Mietzsch, Mauss and Kikuth report synthesis of new anti-malarial - a yellow acridine dye - Atabrine
1940's	Further research into synthetic anti-malarials prompted by malaria outbreaks among British and US troops during World War II
1941	Synthesization of Atabrine on a commercial scale in the US. Widespread use among Allied forces
1940's	Development of two 4-aminoquinoline compounds in Germany - Sontochin and Resochin
	Following further trials, Resochin is ultimately chosen drug and is renamed chloroquine
	ICI study the potential of pyrimidine derivatives as anti-malarials
1945	Curd, Davey and Rose identify proguanil (Paludrine) as a drug with low toxicity and high activity against avian malaria
1951	Further studies of pyrimidine derivatives lead to development of pyrimethamine (Daraprim) by Hitchings and other scientists of the Burroughs Wellcome Company in the US
1950's	Effectiveness of proguanil and pyrimethamine towards *P. falciparum* infections found to be declining
1960	Resistance to chloroquine identified in Colombia with other countries soon to follow
1990's	*See above*

DFID Department for International Development

THE MALARIA FOUNDATION INTERNATIONAL
Global Networking Against Malaria
http://www.malaria.org

Malaria remains one of the biggest killers in the world today. Over one million people die every year and 500 million fall ill. Worst affected are children and pregnant women.

Roll Back Malaria is a new global initiative which aims to halve the number of malaria deaths by 2010 and halve it again by 2015. Roll Back Malaria is a collaboration of governments, the World Health Organisation, international agencies, research institutes and the private sector.

Malaria

"Every 30 seconds, a child somewhere dies of Malaria. It kills indiscriminately, it puts an enormous strain on health services, and prevents the developing world escaping from grinding poverty. The Roll Back Malaria initiative presents a huge opportunity to make a difference."

Secretary of State for International Development
Rt Hon Clare Short MP

International Roll Back Malaria Initiative *Key facts*

Malaria is one of the biggest killers in the world, killing over 1 million people and affecting about half a billion others a year. Nine out of ten deaths occur in Africa.

Attempts to eradicate the disease in the 1950s and 60s failed. Since then malaria has killed more than 40 million people.

Malaria contributes significantly to sustained poverty and untold suffering for 40% of the world's population with pregnant women and children being especially vulnerable.

The Roll Back Malaria initiative was announced by the WHO Director General Elect, Dr Gro Brundtland, on May 13th 1998. It is a global strategy to improve health systems in order to:

enable people to have speedy access to effective treatment for malaria and means of protection from mosquito bites, *enabling national authorities and non governmental organisations* to combat malaria intensifying efforts to develop new products for the prevention and treatment of malaria.

The **Roll Back Malaria** initiative proposes some possible goals: a 50% reduction in malaria deaths by 2010 and halving them again by 2015 using techniques which already exist and need wider dissemination, or which can rapidly be developed. These include:

- **Better treatment of disease through proper diagnosis and treatment**
- **Better protection - use of insecticide treated mosquito nets which promise to cut death rates**
- **Control of mosquitoes - with environmental development and industrial groups**
- **Improved surveillance of disease and the mosquito vectors**

New tools are needed, and researchers and pharmaceutical industry partners will be encouraged to intensify efforts to develop vaccines and new treatments. This will counter rising levels of drug resistance. Social and operational research will also be necessary to ensure that the strategy can be adapted to meet the needs of people and communities.

The Roll Back Malaria initiative will mobilise and co-ordinate a global coalition including leaders from malaria-ridden countries, the World Health Organisation (WHO), United Nations agencies, the World Bank, scientific institutions, private sector bodies and governments world-wide.

The Roll Back Malaria initiative will act as a pathfinder for essential action for overall improvements in the health of people in poorer countries. Health systems will be reinforced so that they can deal not only with malaria but also other major causes of death and disability such as TB, other communicable diseases and unsafe pregnancy.

This is a global initiative - all continents are affected. The spearhead will be in Africa which, through the Heads of State of the Organisation of African Unity countries, called for such an initiative last year. This will be a joint action in involving several international organisations co-ordinated by WHO with resources channelled through a wide range of partners who have shown themselves to be effective. The outcome will be better health sectors, able to address a range of priority health needs of people in poor countries, and much less suffering due to malaria.

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Background Information on Malaria
MFI and DFID
14 May 1998

This information has been gathered by the Malaria Foundation International with contributions from over thirty international medical and scientific experts and from the UK Department for International Development.

EXECUTIVE SUMMARY

Burden of Disease

MALARIA had been eliminated or effectively suppressed in many parts of the world. It is now undergoing a resurgence. It is a public health problem today in more than 90 countries inhabited by some 2,400 million people -- 40 percent of the world's population. Malaria is estimated to cause up to 500 million clinical cases and over one million deaths each year. Every 30 seconds, a child somewhere dies of malaria. In any given year, nearly ten percent of the global population will suffer a case of malaria. Most survive after an illness of 10-20 days. Children are especially vulnerable to malaria. In Africa, where 80% of malaria cases are treated at home, the disease kills one child in twenty before the age of five Pregnant women are also at high risk. There is a fourfold increase in risk of disease and a two-fold increase in death rates. In many African countries about 10% of hospital admissions are for malaria, as are 20-30% of doctor's visits

Resurgence of Malaria

Malaria is returning to areas from which it had been eradicated, and spreading in to new areas, such as Central Asia, and Eastern Europe. More people are now dying of malaria than thirty years ago.

Economic Costs and barriers to development

Over a quarter of a very poor family's income can be absorbed in the cost of malaria treatment, quite apart from the cost of prevention, or the opportunity cost of labour lost to

illness.

Each bout of malaria causes its victim to forego, on average, 12 days of productive output.

Malaria infection can be chronic and unremitting in parts of the world with high transmission intensity, such as coastal Africa. Persons may receive hundreds of infectious mosquito bites a year, with the result they are perpetually weakened by the parasite. Children face particular risks.

People are most at risk of malaria during the warm and rainy seasons; this is usually when there is most agricultural work that needs to be done.

Malaria and fear of malaria prevents investment and tourism into new regions, further hampering economic development.

There are several factors which contribute to this:

- Drug resistance is a growing problem, chloroquine is an extremely safe and cheap drug, but in Asia and an increasing area of Africa and South America the resistance levels are high. In some areas of Asia there is resistance to all the major drugs.
- Mosquitos are developing resistance to the major classes of insecticide which have been used to control the disease.
- Population and demographic changes have resulted in more people moving into densely populated areas, thereby increasing transmission.
- Human environmental changes such as road building, mining, deforestation, and new agricultural and irrigation projects have created new breeding sites.
- Migration, climatic change and the creation of new habitats have all resulted in people who have no natural immunity to the disease being exposed. This results in much higher rates of disease and death.
- In many regions, malaria control programs have deteriorated or been abandoned.

Infection Illness and Disease

The malaria pathogen is not a bacterium; it is not a virus. It is a unicellular parasite.

There are four different species of the malaria parasite. Two are most common. *Plasmodium falciparum*, which is found globally but is commonest in Africa, is the most aggressive species, often killing through coma or anemia. *Plasmodium vivax*, which ranges widely throughout Asia, Africa, the Middle East, Oceania, and the Americas (and is resurgent in Eastern Europe), can cause recurring and debilitating infection, but rarely kills.

Fever is the first symptom. Several hours later, the fever drops and chills set in. Two to four days later, the cycle repeats. More serious forms of malaria can affect the brain and

the kidneys. Progression of symptoms from initial fever to death can take as little as 24 hours.

Much of the long-standing disability from malaria is attributable to the anaemia that it causes.

Reasons for the Resurgence of Malaria

Over the last decades control of malaria has been neglected and under-funded. Until the 1990s major agencies were wary at taking up the challenges posed by malaria because they are difficult.

Many national health ministries need increased technical capacity and financial resources if they are to tackle infectious diseases effectively.

Basic health services, which have been characterized by declining levels of funding, low staff morale and inadequate drug supplies, have been unable to address the challenges of effective diagnosis and prompt treatment.

Pharmaceutical companies have spent relatively little on research.

Research Efforts

The total amount spent on malaria research globally accounting for all governmental charitable and non-governmental sources in 1993 was $84 million.

A vaccine is needed. Development of such a vaccine is complicated by the parasite ability to change its immunological identity, and thereby conceal itself from the immune responses that might otherwise be stimulated by a vaccine.

Vaccines have been tested in animal models and there are eight ongoing clinical trials for vaccines. There are other candidate vaccine in the pipeline.

New drugs are required particularly in areas such as Asia where drug resistance is a major problem. Such drugs must be affordable for poor people.

Epidemiological research is required so that epidemics can better be predicted, and contingency plans made. Social and Operational research is required to ensure that strategies for prevention, treatment, and control are adapted to the situations which occur in each country.

Recent Initiatives on Malaria

The Multilateral Initiative on Malaria began as a joint African-American-European project that brought together representatives from thirty-seven countries, three charities and three intergovernmental agencies in Senegal in 1997. Already it is beginning to increase to the co-ordination of research efforts.

The African Initiative on Malaria responded to the call from the ministers the

Organization of African Unity in 1997. This coalition of national governments, the World Bank, multilateral agencies such as UNICEF and bilateral donors, will be co ordinated by WHO.

The Roll Back Malaria Initiative brings these ongoing efforts together. It was announced by Dr. Gro Harlem Brundtland in her inaugural speech as Director General of WHO on May 13,1998, with the following words:

"I propose that together we Roll Back Malaria. Not as a revamped vertical program but by developing a new health sector wide approach to combat the disease at global, regional and country and local levels.

Why malaria? Many have asked this question. For my part the answer is simple, I have learned it from many in this room and by traveling to your countries, particularly in Africa.

Malaria is the single largest disease in Africa and a primary cause of poverty. Every day 3000 children die from malaria. Every year there are 500 million cases among children and adults.

Who said that infectious diseases were becoming yesterday's problem? The human suffering is unacceptable and so is the economic burden and impediment to progress. Time has come to respond with a new approach. Time has come to Roll Back Malaria.

Why now? Because the call is there. We have enough knowledge, skills and tools to launch a new concerted effort. Africa is responding. African leaders are committing to a renewed effort to control malaria. Africa should be spearheading the project.

I believe we should answer Africa's call and that of other regions if they choose to engage. I will invite a broad range of stakeholders to join us in this initiative, UNICEF, the World Bank, industry, foundations and all others who have a stake, a commitment and a contribution to make.

I encourage the leaders of the G8 countries to answer the call when they meet later this week.

Let me stress: Roll Back Malaria will not exclude work on other diseases. To the contrary. Successful containment is no endpoint. Rolling Back Malaria is no victory unless health systems are equipped to sustain the gains.

That means connecting the services with the primary location for action; the family - the home - and the mother. Efforts against all infectious diseases will benefit. Drawing upon what we learn we will be ready for a fast track on a future Roll Back TB - and a reinvigorated action against HIV/AIDS and tropical diseases."

"MALARIA which had been eliminated or effectively suppressed in many parts of the world, is undergoing a resurgence. It is a public health problem today in more than 90 countries inhabited by some 2,400 million people -- 40 percent of the world's population. Malaria is estimated to cause up to 500 million clinical cases and 2.7 million deaths each year. Every 30 seconds, a child somewhere dies of malaria. The global effects of the disease threaten public health and productivity on a broad scale and impede the progress of many countries toward democracy and prosperity."

Institute of Medicine of the National Academy of Sciences of the United States (1996)

* * * THE HUMAN DIMENSIONS OF MALARIA ARE STAGGERING. It is, by far, the most devastating and deadly parasitic disease in the world. Although an ancient disease, environmental disturbance, malnutrition, and the failure of drugs once used to control the disease have conspired to make death by malaria more frequent now than at any point in history:

- In any given year, nearly ten percent of the global population will suffer a case of malaria. Most survive after an illness of 10-20 days. Many do not.
- Africa is terribly affected, and accounts for over 90% of reported cases of malaria. About 10% of hospital admissions are for malaria, as are 20-30% of doctors' visits. As bad as that is, experts foresee as much as a 20% annual increase in Africa's rate of malaria-related illness and death. No Western disease is nearly so prevalent or growing at anything like that rate.
- Children are especially vulnerable to malaria. In Africa, where 80% of malaria cases are treated at home, the disease kills one child in twenty before the age of five. Globally, the death rate is equal to seven jumbo jets, full of children, crashing every day.
- Pregnant women are also especially at risk. In highly malarious parts of Africa, women are more than four times as likely to suffer clinical attacks of malaria during pregnancy than at other times; but only half as likely to survive bouts of life-threatening illness.
- In comparison to other infectious diseases, malaria kills about as many persons per year as AIDS has done in the last 15 years. About 30 times as many persons die of malaria every day, as died in the infamous Zairian Ebola virus outbreak of 1995.
- Westerners who visit malarious countries, however briefly, are not immune! Several thousand return home from travels each year and are hospitalized with malaria. Travelers have contracted "airport malaria" while waiting on planes that were being refueled in malarious areas.
- Expatriates and soldiers who live abroad are at even greater risk. Malaria was the number one cause of hospitalization among American troops deployed to Somalia; the number two cause among troops in Vietnam (after combat injury); and a leading cause among diplomats, missionaries and aid workers.
- Blood transfusion can also transmit malaria. Two persons in the United States died of malaria in this way in 1997
- Each year, the world over, malaria destroys, through premature death and disability the equivalent of at least 35 million years of healthy, productive human life a figure that dwarfs the human cost of better-recognized infectious diseases such as Ebola or AIDS.

SOURCES: World Health Organization; US Agency for International Development; Wellcome

Trust; Institute of Medicine, National Academy of Sciences (USA); *Transactions, Royal Society of Tropical Medicine and Hygiene* (UK); *Social Science and Medicine*; Centers for Disease Control; Office of the US Army Surgeon General; Harvard Malaria Project; World Bank.

2. THE REEMERGENCE AND SPREAD OF MALARIA

"THE GLOBAL "RE-EMERGENCE" OF MALARIA has several underlying causes. Population and demographic changes have resulted in more people moving into densely populated areas, thereby increasing transmission. Human environmental changes such as road building, mining, deforestation, and new agricultural and irrigation projects...have created new breeding sites... [and] in many regions, malaria control programs have deteriorated or been abandoned." The World Resources Institute; United Nations Environment Programme; United Nations Development Programme, and the World Bank (1998)

* * *

A plague is coming back, and we have only ourselves to blame. In a fight, the worst error is to misestimate a foe, and that is what we did with malaria. By failing to deal resolutely with malaria in the past, scientists and politicians have bequeathed today's children a parasite stronger than what they knew. We are now poised to perpetuate that error and be submerged or fight back.

- Insecticide resistance was the first mistake, the legacy of a scientifically naive, politically uncommitted effort to eradicate malaria in the 1950s and 1960s. Global DDT spraying to kill mosquitoes succeeded in controlling malaria for a time: in only 8 years, Sri Lanka went from a million cases of malaria a year to only seventeen. Then the American Congress cut its funding for spraying, and the mosquito evolved resistance to DDT. Within a decade, malaria rebounded to nearly a million cases a year.
- Drug resistance was the second mistake, the legacy of foolishly overusing antimalarial drugs. Some countries even laced salt with chloroquine, the drug of choice. Errors like that, or the money-saving trick of taking a partial, rather than complete, course of drug treatment, caused the malaria parasite to evolve resistance. Now chloroquine, the cheapest, safest, and most effective drug we have ever known is rapidly losing its effectiveness.
- Environmental changes and human mobility are a third mistake. Industrial works in the tropics, such as mining or logging, create puddles of still water that are the mosquito's dream habitat. Malaria transmission explodes just as a crop of outsiders with no immunity to the disease come into work camps. Indigenous people also suffer unprecedented onslaughts of malaria. Incidence of malaria among Yanomami Indians in the Amazon have leapt almost seventy-fold since contact with industrial works. Now, a quarter of Yanomami die of malaria, in what is reckless genocide by malaria.
- Political ignorance and budget cuts are a fourth mistake. For the Yanomami, who have been brought disease but no outside help because malaria research and control budgets have suffered huge cuts, it may be the last mistake. International health is a sitting duck when politicians balance budgets. The creation of wars and refugees, another politicians' foible, provides conditions ideal to the aggressive spread of malaria among displaced persons.
- In the future, we will still make mistakes. Climate change may be a new threat. The malaria parasite grows faster in warm areas. Even a tiny global warming will push malaria into Africa's urban centers and into temperate zones outside the tropics - places where people have no

immunity and fall easily to malaria. As recently as the early 1900s, malaria cases were 500,000 a year in the south of the US; and it was only in the 1960s that malaria was eradicated from Italy. Europe and the US still suffer a handful of cases each year.

SOURCES: MIT Technology Review; World Health Organization; R. Desowitz, *The Malaria Capers*; L. Garrett, *The Coming Plague*; The World Resources Institute, United Nations Environment Programme, United Nations Development Programme, and the World Bank; Institute of Medicine, National Academy of Sciences (USA).

3. ECONOMIC COSTS AND BARRIERS TO DEVELOPMENT

"MALARIA HAS BEEN CALLED THE "LAZINESS" DISEASE because it is so debilitating. The most prevalent disease in poor rural regions, malaria produces recurrent infections with attacks of fever in warm and rainy seasons, just when workers are needed to collect crops."

The World Resources Institute; United Nations Environment Programme; United Nations Development Programme, and the World Bank (1998)

"WHEN A SUBSTANTIAL PROPORTION of a country's population is ill with malaria for five or six months each year, sustained economic development is very difficult to achieve. Countries thus

compromised cannot easily become active trading partners...nor are they positioned to decrease their dependence on foreign aid. Similarly, when child survival is threatened by malaria and other infectious diseases, family planning and environmental quality are simply not priorities."

Institute of Medicine of the National Academy of Sciences (1996)

* * * MALARIA IS A "DISEASE TAX" ON ECONOMIC AND HUMAN DEVELOPMENT. To put it simply, a person ill for weeks or months at a time is not a productive person. In afflicting entire races and nations, malaria squelches development; discourages inward capital investment; stultifies global trade; and generally, depresses the standard and quality of life for the world's most disadvantaged persons. Yet the marginal cost of reversing malaria's toll is, comparatively speaking, small.

- Over a quarter of a very poor family's income can be absorbed in the cost of malaria treatment, quite apart from the cost of prevention, or the opportunity cost of labour lost to illness.
- Each bout of malaria causes its victim to forego, on average, 12 days of productive output.
- Malaria infection can be chronic and unremitting in highly diseased parts of the world, such as Africa. Persons may receive hundreds of infectious mosquito bites a year, with the result they are perpetually weakened by the parasite.
- Cash estimates of malaria's direct costs underestimate the problem because lost income is only the tip of the iceberg. If each day of malaria-related disability were valued at $1 of lost income, then malaria's annual cost is about $13 billion globally. But if we add in the value of lost social services, such as care for the

elderly (when the young die), or childrearing (when parents die) then the cost of malaria is very much greater.

- Attacking global diseases is a bargain. Since smallpox was eradicated in 1977, the total US total investment of $32 million is returned to the US as savings every 26 days! Every dollar spent on the measles, mumps and rubella vaccine results in a $21 savings later.

SOURCES: Tropical Medicine and Parasitology; Institute of Medicine, National Academy of Sciences (USA); MIT Technology Review; World Bank; National Science and Technology Council, White House Office of Science and Technology Policy.

4. INFECTION, ILLNESS AND DISEASE

"FOR CENTURIES distancing beyond recorded history, malaria has been a pregnant ladykiller. Malaria also kills the children; in regions of intense transmission, 40 percent of the toddlers may die of acute malaria. Malaria also kills the immunologically "unsalted" adult migrants from teeming Third World cities who pioneer new agricultural lands, soldiers of the Western world battling to save democracy in tropical nations, tourists, businessmen. In 1990 the age of rocket ships and genetic engineering 250 million people will get malaria and at least 2.5 million will die of the infection - needless deaths. Malaria is not an AIDS; the curative antimalarial drugs are available. Malaria is not like cancer; the most intimate details of malaria's causation are known. Malaria is not like the epidemic of drug addiction; given the resources, successful antimalarial campaigns can be implemented."

Robert Desowitz, *The Malaria Capers* (1991)

"THE BLIGHT OF BENIN. The blight of Benin. Few go out but many come in"
West African colonists" lament, circa nineteenth century.

* * * THE MALARIA PARASITE IS A TRICKSTER. It is not a bacterium; it is not a virus. It is a form of unicellular life as sophisticated as the cells of our bodies. It is the evil opposite of our immune cells, and that makes it a nasty foe. Passing from person to person via the bloody feasts of mosquitoes, the parasite assumes a different "disguise" with each infection, dodging the victim's immune system and whatever experience it had with malaria in the past. In brief, the parasite has perfected the trick, over millions of years and trillions of infections, of waylaying us like neophytes every single time.

- There are four different species of malaria parasite that go by the collective name of *Plasmodium*. Two are most common. *Plasmodium falciparum*, which is found globally but is commonest in Africa, is the most aggressive species, often killing by coma or anemia. *Plasmodium vivax*, which ranges widely throughout Asia, Africa, the Middle East, Oceania, and the Americas, can cause recurring and debilitating infection, but rarely kills.
- Not all persons with the parasite have disease, but some are carriers without symptoms. A mosquito can draw blood from these people, and some weeks later, transmit the parasite to another person, who may be more vulnerable. The

parasite takes refuge in that person's liver, and later erupts into the blood, where it invades his or her red blood cells and begins to replicate.

- Fever is the first symptom. The fever moves in cycles as the parasites destroy one bunch of blood cells and, in larger numbers than before, take over another bunch. At its peak, a person's fever can soar to 41°C (106°F). Several hours later, the fever drops and chills set in. Two to four days later, the cycle repeats.
- Cerebral malaria is the most dreaded form of the disease, and this is unique to *P. falciparum*. Red blood cells infected by the parasite are sticky and can gum up the capillaries of the brain. The victim enters a coma, and if he is lucky enough to return, brain damage can be the result.
- Death can strike in as little as 24 hours from first symptoms: or in less time than it takes to get from a village to a clinic! Thus, better access to clinics is essential to turning the tide on malaria.
- Even at a clinic, death is nearby. Village clinics are almost always poorly equipped. The clinic is unlikely to own a microscope, which is essential to diagnose malaria. If the clinic has antimalarial drugs, they may be useless because increasingly the parasite is likely to be drug resistant. And in the case of cerebral malaria, sterile intravenous equipment is needed, a tall order in remote Africa.
- Anemia is another threat. The parasite's cyclical attacks on red blood cells can result in death by blood loss. As a last-ditch effort, the victim is sometimes given a transfusion. Without a way to test the donor's blood for HIV, if the victim survives malaria, he or she will be lucky to not get AIDS.
- Pregnant women are malaria's easiest prey. The normal weakening of the immune system during pregnancy makes infection more likely, and the routine anemia of pregnancy gives the parasite a deadly leg-up. Pregnant women are four times as likely to get the disease, and half as likely to survive cerebral malaria. If they do, their fetus may not: the extreme fevers often cause spontaneous abortion.

SOURCES: World Health Organization; Institute of Medicine, National Academy of Sciences (USA); *Transactions, Royal Society of Tropical Medicine and Hygiene* (UK); *Social Science and Medicine*; *Bruce-Chwatt's Essential Malariology*.

5. OBSTACLES TO EFFECTIVE CONTROL

A. WEAK POLITICAL COMMITMENT

"THE UNFORTUNATE FACT is that foresight and compassion are no match for politics and profits in setting priorities for disease research. When malaria comes here, we'll seriously get to work on it. But sadly, not until then."

Daniel S. Greenberg in *The Washington Post* (1998)

- There is the healthy, wealthy world; and the ill, poor nowhere. In sub-Saharan Africa alone, malaria destroys 76% more years of productive life than do all cancers in all economically developed countries. Yet the US spends fifty times as much on cancer research as malaria research. This is typical: in Canada, the difference is forty-fold.
- Vanquishing malaria is like fitting together a puzzle. First you lay out the pieces:

talking about the problem; training scientists and doctors; providing research funding. Then you build the edges: introducing control measures to the field; teaching communities to use them; studying how the disease fights back against control; designing new drugs and vaccines. Then you fill the center: testing new drugs and vaccines; sharing those that work. The last piece makes a picture of health. But it takes political will, in the beginning, to open the puzzle box!

- Africa is asking for that political will; is anyone listening? In 1997, the 53 African heads of state passed a resolution at the Organization of African Unity, to ask for help against malaria. Without scientific tools themselves, African countries must rely on developed countries to hear their plea.
- With a commitment, disease control is possible. Politicians acted to eradicate smallpox from the face of the earth for about $300 million. In a campaign of less than a decade, 97% of cases of guinea worm were eliminated it will be driven extinct within five years. In just one day in 1997, India vaccinated 130 million children against polio. Similar "vaccination days", paid for by governments, the WHO and groups like the Rotary Club, will destroy this killer of children by the year 2000.

SOURCES: World Bank; Wellcome Trust; Medical Research Council (Canada); Organization of African Unity; Carter Center; Rotary International.

B. THE LOOMING CRISIS OF DRUG RESISTANCE

"TODAY, RESISTANCE IS EMERGING AND SPREADING faster than new drugs can be developed...Given the speed with which parasites are becoming resistant and the length of time required to develop new drugs (even accelerated development takes 5 to 10 years from discovery to clinic), we face a looming crisis: multidrug-resistant malaria with no safe, effective alternatives for treatment. This problem exists today in Southeast Asia and will occur in most other malaria-endemic areas within the next decade."

Massachusetts Institute of Technology, *Technology Review* (1997)

"NOT A SINGLE major Western pharmaceutical company is now developing new drugs for malaria."

Institute of Medicine of the National Academy of Sciences of the United States (1997)

- The "good" strains of malaria are difficult to treat; the "bad" ones are impossible. Careless drug use has caused malaria parasites to evolve survival strategies against drugs. In most areas, malaria parasites resist at least one drug. In others, they resist all known drugs. There are no failsafe treatments, a state of affairs not known since the discovery of quinine in the 17th century.
- Malaria prevention is also in jeopardy. Travelers to malarious areas take antimalarial drugs to avoid getting the disease, but the parasite can resist prophylactic drugs too. There is no prescription that guarantees a traveler absolute safety from malaria.
- Things are getting worse, not better. Today, only government and university labs

do malaria drug research, on a budget under that of the 1980s. The US military has invented most of the drugs used in the last 50 years, yet its drug research program advances on just $5 million a year, and even this is threatened by cuts.

SOURCES: WHO; Journal of the American Medical Association; New Scientist; Nature.

C. THE QUEST FOR A VACCINE

"...A VACCINE that can prevent illness and death of malaria could be one of the most important advances in medicine, with the potential for improving the lives of hundreds of millions of people." [emphasis in original]

"IN SPITE OF GROWING SCIENTIFIC OPTIMISM, the pace of vaccine development appears to be slowing because of diminishing public funds, fragmented public sector efforts, and limited interest within the vaccine industry."

Both from Institute of Medicine of the National Academy of Sciences (1996)

FINDING A CHEAP, EFFECTIVE MALARIA VACCINE IS THE HOLY GRAIL OF RESEARCH. Unlike drugs that prevent or treat the disease only so long as they are taken, vaccines confer enduring, even life-long, immunity to disease. If a good vaccine is distributed widely enough, it is even possible to forever wipe the disease from the face of the earth.

- Researchers have yet to develop a successful malaria vaccine in humans, although they have succeeded in immunizing many types of animals, from rats to monkeys. The last step is proving elusive, even though studies over 20 years ago proved that humans can be successfully immunized in the laboratory.
- The barriers to vaccine development are not so much technical as financial. Although eight clinical trials are now underway globally, many other candidate vaccines are kept out of trials because research funding is so petty. US military scientists alone possesses a half dozen candidate vaccines ready for human testing, but with a budget of just $4 million a year, they cannot do the job. European, Australian, and South American labs are in a similar bind.

SOURCES: *Parasitology Today*; Military Infectious Diseases Research Program, US Department of Defence; *New York Times*; *Nature*.

D. POOR COORDINATION OF RESEARCH

"THE URGENT NEED is to put malaria on the scientific, media and political agenda, and in particular to identify it as a priority for research, both in the developed North and in those areas of the South where the disease is endemic... We recognize that the control of malaria in Africa will require a long-term collaboration between scientists in the North and South...[and] commitments from the industrialized countries to funding, and from

African leaders to support scientist and health and research infrastructures in their countries."

Scientific representatives of seven countries, the World Bank, the World Health Organization, Organization of African Unity, and the Wellcome Trust (1997)

NO ONE COUNTRY WILL SOLVE MALARIA. A disease endemic to 100 countries needs multilateral effort to conquer. Rich states must give of their funds and technological expertise; poor states must supply facilities and cooperate, especially in field research.

- The Multilateral Initiative on Malaria (MIM) began as a joint African-American-European project that brought together representatives from thirty-seven countries, three charities and three intergovernmental agencies in Senegal in 1997. Despite a plea for joint action to save lives in Africa, countries have so far responded with token funding donations, nowhere near the hundreds of millions of dollars now needed and which could become available with a serious global commitment.

SOURCES: Institute of Medicine, National Academy of Sciences (USA); Ralph Nader; World Health Organization.

6. OPTIMISM FOR DISEASE CONTROL: TOOLS IN HAND

"CONSIDERING THESE DIVERSE UNDERLYING FACTORS makes it clear no single strategy will be effective in reducing the burden of malaria. A comprehensive malaria control strategy requires three interdependent and complementary components: disease management, surveillance, and prevention, including environmental management."

The World Resources Institute; United Nations Environment Programme; United Nations Development Programme, and the World Bank (1998)

THERE ARE THINGS WE CAN DO TODAY TO ATTACK MALARIA. Though we need to research new tools, our existing tools can already save many, probably even most, lives.

A. BASIC RULES OF MALARIA CONTROL

- Taking a bite out of the mosquito. If people are taught how, they can wage war on mosquitoes: by filling ditches or covering containers where water stagnates and mosquitoes breed; by stocking ponds with fish that eat mosquito eggs; by using insecticides judiciously and in the right places; by insect-screening their homes; and by planting water-hungry trees to dry out muddy soils. These are just a few of the measures to destroy mosquito breeding sites.
- Managing the illness. Like many diseases, malaria is less likely to kill if it is detected early and treatment is started at once. This means families must be taught to recognize the telltale signs of malaria, especially in children; and well-staffed, well-stocked clinics must be nearby to give medical care. Considering that the disease can progress in 24 hours from first symptoms to death, a dense

network of caregivers and clinics throughout the countryside is a must too many children die now in the arduous journey to a clinic.
- Tracking the disease, and where it will strike next. Much of malaria's bite can be mitigated if it is anticipated first. For instance, by tracking the spread of drug resistant parasites, prescriptions can be changed before people die because they are given ineffective drugs. Keeping an eye out for new environmental changes or refugee movements means preventative or curative resources can be sent to meet the disease before an epidemic begins.

SOURCES: World Health Organization;.US Agency for International Development; The World Resources Institute, United Nations Environment Programme, United Nations Development Programme, and the World Bank.

B. BEDNETS: BITING BACK AT THE MOSQUITO

- Taking care of number one - Avoiding mosquito bites, is a cheap and very effective way to reduce deaths. Mosquitoes bite at night, by sleeping under a mosquito net impregnated with a natural, biodegradable insecticide derived from chrysanthemums lowers one's risk of disease greatly.
- Saving children's lives for a few dollars. More than 20 studies of bednets have proven that they are effective at reducing child mortality, not only from malaria, but from other diseases too. In studies, bednets have reduced mortality by at least 20%, and as much as 63%. According to WHO, if all of Africa's children used bednets, about half a million lives a year could potentially be saved.
- Bednets are so cheap, they can be given away. Nets cost $5-10, and a year's natural insecticide under $1, making bednet donation programs cheap and well within the means of governments and large companies. With will and commitment properly managed integrated programmes with the incorporation of bednets, better use of available drugs, and further needed research could all be a reality.

SOURCES: International Development Research Centre (Canada). World Health Organization; *Annals of Tropical Medicine and Parasitology*.

7. SCARCITY OF FUNDING FOR RESEARCH:

"GLOBAL INVESTMENT IN MALARIA RESEARCH over the past ten years has been very low compared with other disease areas, and appears to be declining further. Expressed as investment in research per death, malaria research ? at approximately $42 per fatal case receives less funding, by one or two orders of magnitude, than other diseases such as cancer, HIV/AIDS or asthma."

The Wellcome Trust (1996)
"RICH COUNTRIES STUDY THE DISEASES THAT AFFLICT THEIR CITIZENS. For the ailments of the poor world, they offer sympathy and perhaps a few bucks."
Daniel S. Greenberg in *The Washington Post* (1998)

THE LACK OF MALARIA RESEARCH FUNDING IS INSTITUTIONALISED NEGLIGENCE: Governments and industry have cut malaria research spending, often radically, in an epoch of increasing disease prevalence, and decreasing options for disease treatment or control.

- The total amount spent on malaria research globally accounting for all governmental, charitable, and non-governmental sources in 1993 was about $84 million. By contrast, a single agency of the US Government will spend about $2.5 billion on cancer research this year.
- Pharmaceutical companies have malaria research, though the need (and their profits) is greater than ever. Currently there is little activity by major Western pharmaceutical company's in developing new drugs for malaria.
- As we approach the millennium the global malaria research budget is, in real terms, smaller than it was in the 1980s.
- Subsidies into lives saved: for the price of a single year's subsidies to its tobacco farmers, the European Union could support the global malaria research program until the year 2009. At present rates, 30 million people (equal to the populations of Belgium, Denmark, Greece, and Ireland combined) will die of malaria between now and that date.
- Swords into plowshares: for the price of a single B-2 Stealth Bomber, the United States could support its current malaria research program until the year 2034, or the global program until 2016.

SOURCES: The Wellcome Trust; *The Washington Post*; Institute of Medicine, National Academy of Sciences (USA); *Nature*; Center for Study of Responsive Law (Washington); EC Directorate General for Agriculture; Central Intelligence Agency.

8. HUMANITY'S CHALLENGE

"WE COME THEN TO SOCIAL INTELLIGENCE as our remaining option to counter the evolutionary drives of the microbial world. That intelligence must include a profound respect for the ecological factors that enhance our vulnerability... [The] preponderant changes are the sheer expansion of our species, with high population densities, and much the worse, egregiously stratified by standards of economics, nutrition, housing and public health. At the same time, we have unprecedented mixing of people: a million passengers a day cross national boundaries by air... One could hardly have concocted a better-calculated recipe for a tinderbox, as AIDS already harshly teaches. From this perspective, we have never been more vulnerable; this vulnerability must be matched against the extraordinary sophistication of the science and technology that we are, in principle, able to pit against these threats."

Dr. Joshua Lederberg, Nobel Laureate in Medicine, and father of molecular genetics
Journal of the American Medical Association (1996)

"DUTY arises from our potential control over the course of events."

Professor Alfred North Whitehead, Philosopher and scientist

THE SCIENTIFIC INTELLIGENCE IS READY. WHAT ABOUT THE POLITICAL? There is no doubt that our present technologies can yield effective drugs, vaccines, and other clinical tools to combat malaria. There is also no doubt that while we develop those tools, environmental and personal control measures like bednets can save lives. The only question is whether the political intelligence can be found to fund malaria research and control decently, or whether malaria will fester, a totem of humanity's ignorance.

- Roll Back Malaria On March 13, 1998, the World Health Organization announced a global campaign, allying the WHO, the World Bank and governments of the developing and developed world alike, to Roll Back Malaria. The program aims to halve malaria deaths by 2010, and have them again by 2015, primarily through rebuilding health care and malaria control in developing countries. It remains to be seen whether governments respond with money to Roll Back Malaria, or just words.

The pressure must be kept on! Because it is such a challenging disease, it is difficult to predict how the war against malaria will progress, except in the case that citizens do not act, and nothing happens. Speak or write to your politicians; tell them that the health of poor children matters no less than rich children; demand that your country support health before weapons, and lives before corporate subsidies; watch that you are heard; and remember when you vote!

MALARIA FOUNDATION INTERNATIONAL

MALARIA FOUNDATION INTERNATIONAL

Global Networking Against Malaria

The Drive Against Malaria

In 1998, in partnership with the MFI and MEMISA, British global explorer David Robertson launched a great challenge: to circumnavigate the globe in a four-wheel drive vehicle to draw attention to the growing danger of malaria. MFI assisted Mr. Robertson in raising public and political awareness in countries throughout Africa and Europe. To date he has visited 48 countries. Having helped David get off to a good start, the MFI wishes him well in his travels!

South Africa is country number 27 as Africa leg begins. (*press release* 17 March 1999)

Rotarians Against Malaria: Letter to fellow Rotarians asking for support for DAM

Statement from David Nabarro of WH0 (World Health Organization):

"Well I just want to say that you are absolutely, vitally important to ROLL BACK MALARIA. In ten years' time we are going to see the halving in the number of people who die as the result of the malaria parasite. This will be as a result of an enormous global movement from lots of organizations' work together in partnership and it's a result of you, David and the Drive Against Malaria group sponsored by MEMISA and the Malaria Foundation International that will make this possible. You will transform the landscape of community action against malaria and I look forward to following your progress with very great interest!!! Good Luck!

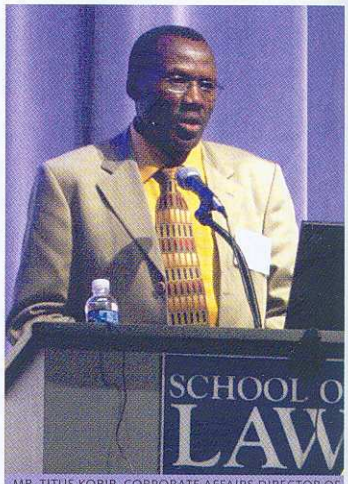
MALARIA PIXELS: DRS. MARY GALINSKI,WEN KILAMA AND WIL MILHOUS BRING THEIR SUPPORT BEHIND THE NEW "DUNK MALARIA" PROJECT WITH LANCE LAIFER AND STAR BASKETBALL PLAYER STEFFOND JOHNSON REVELING IN THE MOMENT.

BY SAM CHERRIBI |

Malaria

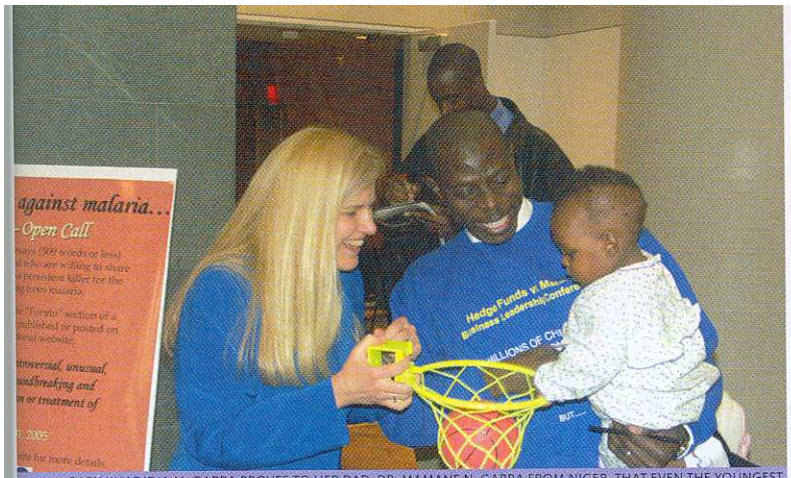
Renewed hope for eradication

"Hedge Funds vs. Malaria" Business Leadership Conference Resonates at top US Universities with Malaria Foundation International Sponsorship. GVA reports.



MR. TITUS KORIR, CORPORATE AFFAIRS DIRECTOR OF JAMES FINLAY, LTD SPEAKS ON BEHALF OF MFI'S STUDENT LEADERS AGAINST MALARIA (SLAM) PROJECT.SCHOOLS IN HIS COMPANY'S COMMUNITY IN KENYA ARE DEVELOPING BROTHER-SISTER ELATIONSHIPS WITH SCHOOLS IN THE UNITED STATES, WITH THE AIM TO REDUCE THE BURDEN OF DISEASE THROUGH EDUCATION AND AWARENESS.

A new and unwavering call is being made to the public, like never before, to wake up and hear the cries of 3,000 children dying each day from malaria. It started in New York City, one week after First Lady Laura Bush addressed dinner guests on September 14, 2005 at the Waldorf Astoria with her featured speech entitled "Fighting Malaria in Africa: Taking Action, Building Partnerships". The first annual "Hedge Funds vs. Malaria" Business Leadership Conference was held at the Marriott Marquis on September 20, 2005. Dr. Mary R. Galinski, Founder and President of the Malaria Foundation International (MFI) and a member of the faculty of Emory University's School of Medicine in Atlanta, Georgia was among the guests at both events. A few weeks later she and her husband Dr. John W. Barnwell, a Senior Biomedical Research Service Scientist and malaria expert at the Centers for Disease Control and Prevention (CDC), were invited by Steffond Johnson to attend the "3rd Annual Legends of Basketball Extravaganza", the annual convention for retired NBA basketball players. The culmination of these events, one after the other, set the pace for Dr. Galinski to realize her dream for the Malaria Foundation International to engage the public in the fight against this disease. "The world has been experiencing an ongoing disaster with a blind eye, and we need strong political leaders, business and marketing experts, sports and entertainment figures, leading financial supporters and others to help jolt the world into action against this disease," said Dr. Galinski. "Malaria is entirely preventable and treatable, yet the estimated 500 million suffering each year from this disease have not had an audience commensurate with the scope of the problem.



BABY KHADIDJA M. GARBA PROVES TO HER DAD, DR. MAMANE N. GARBA FROM NIGER, THAT EVEN THE YOUNGEST AMONG US CAN FIGHT MALARIA, AS SHE DUNKS A BASKET FOR THE "DUNK MALARIA" FUNDRAISING INITIATIVE.

CHARISMATIC ADVENTURER AND EXPLORER MR. DAVID ROBERTSON FROM ENGLAND SHARED HIS DREAM OF BRINGING HIS "DRIVE AGAINST MALARIA" CAMPAIGN TO THE UNITED STATES AND ENLIGHTENING AMERICANS CITY BY CITY, AND TOWN BY TOWN WITH A BASIC UNDERSTANDING AND KNOWLEDGE ABOUT MALARIA. DAVID SPOKE ABOUT HIS PROGRESS TO DATE WITH THE MFI'S SUPPORT TRAVELING IN 57 EUROPEAN AND AFRICAN COUNTRIES.

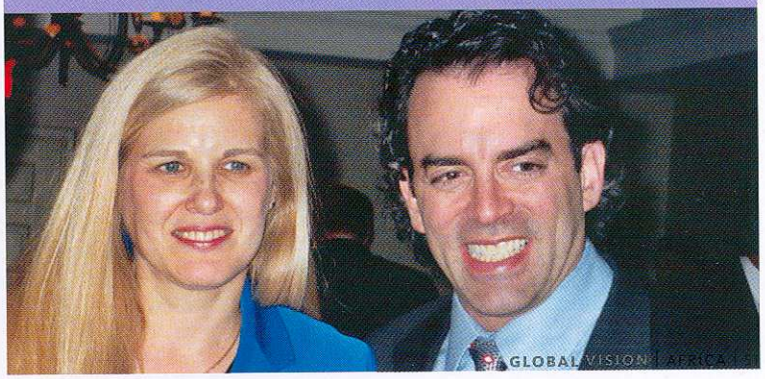
Millions of people are suffering and dying, mostly children, and we believe that once individuals and organizations understand what we are dealing with and how they can help, that more and more people will get involved and become part of a global solution."

As a scientist whose career has been dedicated to malaria research, Dr. Galinski knows the value of discovery in the equation. "We make discoveries in the laboratory, literally each day," says Dr. Galinski. "Yet malaria is a complex parasitic disease, and the actual development and testing of malaria vaccines and new drugs are great challenges requiring large resource pools and research consortiums." She added, "We are extremely grateful for the recent interest from the Bill and Melinda Gates Foundation, Exxon Mobile and others, which is helping to address these major unmet needs. At the same time, we must be sure the world remains cognizant of the realities of malaria and the challenges we face. We do not have a malaria vaccine yet, and the first developed will not be the total solution. There are four species of the malaria parasite, known as Plasmodium, and each has plenty of diversity and immune evasion strategies. While hoped-for malaria vaccines are being developed, their actual implementation and confirmed value in the fight against malaria remain uncertain. Thankfully, new drugs and drug combinations are being produced and tested to replace ineffective compounds, insecticide treated nets show promise as a preventative measure, and DDT is once again being welcomed on the scene to kill or deter the mosquitoes that transmit the disease. The world can team up now to help fight the disease with the goal of immediate and sustainable results."

With this conviction, the Malaria Foundation International with Dr. Galinski's leadership co-organized the First Annual Atlanta "Hedge Funds vs. Malaria" Business Leadership Conference at Emory University on December 6, 2005, in partnership with Mr. Lance Laifer, co-founder of the conference series. The aim was to reach out to a broad audience and involve faculty, students and administrators across campus. The conference was also promoted within the business community to seek marketing wisdom and meet future fundraising goals. The event, held at Emory University's School of Law, garnered campus wide support, including from Emory's President James Wagner. World malaria leaders included Professor Wen Kilama, Founder and Managing Trustee of the African Malaria Network Trust based in Tanzania, Dr. Wil Milhous, Chief Science Officer for Therapeutics at the Walter Reed Army Institute of Research (WRAIR) in Maryland, and Professor Emeritus Robert S. Desowitz, scientist and author from North Carolina. Several press releases, the full program, speaker biosketches and the event's video webcast can be found at the MFI's website: www.malaria.org. In a few captivating hours, the public can now view the conference webcast and gain a good general understanding of malaria and ideas on how they can help. Minimally, one can 'shoot a basket' to participate in the world's "Dunk Malaria" project, which was launched by Lance Laifer at the event. Other projects highlighted at the conference include Student Leaders Against Malaria (SLAM), Drive Against Malaria (DAM), a Malaria Essay Contest and Malaria Free Zone (MFZ) initiatives. Ultimately, the conference aims to raise several million dollars to help tackle the disease each year, and support the foundation in developing new projects. |

The Malaria Foundation International is paving the way for the world to team up against malaria. The MFI seeks business partners to support innovative projects that can involve the masses: students, teachers, church groups, community organizations, business health advocates, etc. Anyone outraged about the status quo, where 3,000 children die daily of a preventable and treatable disease, can join the fight by supporting or participating in Malaria Projects lead by Malaria Project Pioneers (MPPs), a name coined by the MFI. As an advocate for malaria research and development, the MFI also aims to support malaria research projects and continue its role as a leading advocate for the most effective application of currently available methods of controlling the disease. Now more than ever, the public can get involved in a growing number of opportunities to tackle malaria. The MFI welcomes you to www.malaria.org as a friend and supporter.

DR. MARY GALINSKI AND MR. LANCE LAIFER (HEDGE FUNDS)



MALARIA FOUNDATION INTERNATIONAL

OUR CAMPAIGN TO PREVENT A BAN OF DDT
FOR MALARIA CONTROL HAS BEEN SUCCESSFUL!
Thanks to all!

Further important progress is now being carried out by the Africa Fighting Malaria Organization - sign their "Kill Malarial Mosquitoes Now" declaration.

Dear Colleagues

At the end of this long and successful campaign, the Malaria Foundation International (MFI) and the Malaria Project (MP), led by Amir Attaran, would like to both thank and congratulate you and the many parties for valuable assistance that helped to successfully obtain an exemption for DDT at the INC 5 POP's negotiations recently in South Africa.

In particular, we thank the over 400 doctors and scientists from 63 countries, who lent strong support last year when this issue was first brought to the attention of the scientific community. It was due only to this strong support of yourselves, voiced together with others in the public health community, that DDT was not slated for elimination along with the 11 other chemicals on the treaty.

This outcome will save many lives, and it also demonstrates the power of coherent advocacy in achieving public health goals, which is a critical function served by the Malaria Foundation International.

In March 1999, the MFI and the MP wrote an open letter to treaty delegates arguing against a DDT ban without replacement. We thank the following SIGNATORIES for their support.

READ THE LETTER THAT WAS PRESENTED TO THE DELEGATES
English English (pdf) French French (pdf)

Background information on why the MFI has supported an eventual but not immediate ban of DDT:

In certain situations [see KwaZulu-Natal and Ethiopia] there are few effective or affordable alternatives. This puts hundreds of thousands of lives at risk from malaria - in countries where DDT is used to spray homes to block transmission of malaria.

Malaria and leishmaniasis are diseases that are in resurgence in many parts of the world. Diminished control efforts are, at least in part, responsible for this resurgence (Roberts et al. 1997, Roberts et al. 2000, Baird 2000).

The MFI has supported an eventual (not immediate) ban, with the proviso that an effective and affordable replacement is found before DDT is banned.

DDT is one tool of many in the malaria control worker's toolbox. The reason that it is being discussed at this site is that, unlike other tools, there is an imminent danger of it being taken away. This puts not just health, but lives, at stake. The MFI wants to see *all* possible tools for malaria control be readily available, because malaria is a serious, resurgent problem with drug resistance and increasing numbers of illnesses and deaths.

1. Baird, J.K. 2000. Resurgent malaria at the millennium: control strategies in crisis. Drugs. 59(4):719-743. Abstract.
2. Roberts, D.R., L.L. Laughlin, P. Hsheih, and L. Legters. 1997. DDT, global strategies, and a malaria control crisis in South America. Emerg. Infect. Dis. 3:295-302.
3. Roberts, D.R., S.Manguin, and J. Mouchet. 2000. DDT house spraying and re-emerging malaria. Lancet. 356: 330-332.

Further details about the negotiations:

At 7:28 am on Sunday, 10 December 2000, the delegates in Johannesburg, South Africa, approved a treaty allowing for the continued use of DDT in disease vector control as the United Nations Environment Program concluded the fifth and FINAL round of negotiations on a treaty to ban persistent organic pollutants. The official mandate of the treaty was to "reduce and/or eliminate" twelve POPs, of which DDT was one. This led groups such as Greenpeace, World Wildlife Fund, Physicians for Social Responsibility and over 300 other environmental organizations to advocate for a total DDT ban, starting as early as 2007 in some cases. Although the open letter you signed made considerable progress in persuading these environmental groups to change their views, it was only the diplomats and delegates of 120 countries at the Johannesburg negotiations who could take the final decision. I am delighted to report to you that They decided that DDT is a unique case, and whereas the other eleven POPs dealt with by the treaty are on a list to be "prohibited or eliminated" (Annex A of the treaty), DDT alone is on a list to be merely "restricted" (Annex B), with the primary restriction being that DDT use in agriculture is hereby eliminated. The future public health uses of DDT are safeguarded by a "DDT exemption" written into the treaty. That exemption:

(1) restricts DDT use and production to disease vector control only (not agriculture);
(2) requires countries using DDT to follow WHO guidelines for disease vector control;
(3) requires countries to notify WHO if they use DDT;
(4) requires rich countries to pay the "agreed incremental costs" of more expensive alternatives to DDT (this is located elsewhere in the treaty); and
(5) encourages rich countries to support research and development of alternatives to DDT; and having said this, what the treaty does NOT require is equally important:

(1) it does NOT require a country to notify WHO before it sprays DDT, so in an epidemic a country may spray first and report to WHO later;
(2) it does NOT require a country to obtain WHO's approval at any time;
(3) it does NOT require poor countries to bear the added cost of alternatives to DDT;
(4) it does NOT set a deadline by which countries must stop using or producing DDT; and
(5) it does NOT restrict DDT use to malaria control, but allows for controlling any vector-borne disease.

The outcome of the treaty is arguably better than the status quo going into the negotiations over two years ago. For the first time, there is now an insecticide which is restricted to vector control only, meaning that the selection of resistant mosquitoes will be slower than before.

Also, there is a clear procedure that endemic countries may follow to use DDT, and having done so, they have the RIGHT at international law to use DDT, without pressure from the developed countries or international institutions who have in the past threatened them against doing so.

Finally, it provides a legal understanding that rich countries should do more to research and develop alternative control measures for malaria, with the goal of "decreasing the human and economic burden of disease". This will, we hope, translate into additional funds for malaria research and control. The provisional text of the DDT exemption (Annex B) may be read here.

Respectfully submitted by Dr. Amir Attaran

Malaria Research Network

Invitation Letter

January 1997

Dear Colleague,

For some time now, a number of us in the malaria research community have felt the need for greater communication and collaboration in this field. We believe that new approaches and new partnerships, both at a national and an international level, are required to address the complex questions posed by malaria. As an example of such novel interactions, we believe that electronic linkage of malaria investigators can enhance sharing of information, exchange of ideas and reagents, promotion of multidisciplinary collaboration, and the optimum use of available resources.

With this in mind, we have initiated the Malaria Research Network (MRN). In contrast to other electronic activities, this will not be an open discussion forum, but, rather, a private network composed mainly of scientists conducting research on malaria. The MRN is founded on the concepts of *open communication*, *democratic governance*, and *collegial interactions*. Its maintenance and activities will be governed by an elected and rotating group termed the MRN Management and Oversight Committee (MOC)**.** The development of the MRN has been sponsored by the Malaria Foundation, and Co-Sponsors are currently being sought to help support this initiative.

Then MRN has several goals and objectives:

1. The most important goal is to promote and facilitate discussions and collaboration among malaria researchers, regardless of their professional affiliation. This will be accomplished largely through the activities of a number of chaired scientific "working groups," each of which will sponsor a series of "topic discussion" sessions. MRN working group and topic discussion sessions will be conducted primarily on the Internet at this site, although as it is deemed useful, we hope to obtain support for periodic face-to-face meetings as well. Working groups will be organized primarily around research disciplines, e.g., Immunology and Vaccines, Vector Biology, etc., although we anticipate a working group concerning Mechanisms for Cooperation and Support as well. To discourage casual participation, individuals must apply for admission to one or more working groups and provide evidence of professional involvement in the field of malaria, e.g., as a primary investigator/laboratory head, or as a graduate or post-graduate trainee. Active participation in working groups will require admission by the MOC and an assigned personal password.

Working group chairs will recruit topic discussion leaders who will be responsible for setting up electronic meetings organized around selected topics. Introductions, reading lists, and summaries may

be provided to maximize the usefulness of the discussions, and, at times, experts from related areas may be called in to join selected topic discussion meetings. All topic discussions will be archived for one year. In addition, to preserve intellectual property rights while encouraging open communication among MRN members, selected contributions will be time/date stamped and archived for seven years. This setup is designed to be a catalyst for informative multidisciplinary working sessions.

2. Another goal of the MRN is to provide a central electronic forum for sharing information relevant to the malaria research community. This includes announcements of meetings or other programs, special funding opportunities, and important information/updates concerning national or international efforts in areas of malaria research or control. This aspect of the MRN will be open to anyone with Internet access. Such a central forum is particularly important at this time while there are many developments in this field, such as the Malaria Genome Project, new Malaria Initiatives in Africa, the Burroughs Wellcome Fund Malaria Initiative, Malaria Vaccine Progress, etc., which are of interest to a wide audience.

The accompanying web page prototypes are introductory - the actual Malaria Research Network database will open shortly. If you are interested in joining this international program, we invite you to revisit this site for updated information on the membership application process. Also, please share this information with students and colleagues who may be interested in participating. We recognize that at this point in time, investigators in some areas of the world may not be able to access the World Wide Web and consequently will be unable to join and actively participate. However, rapid changes in technology over the next few years will likely enable the involvement of malaria scientists throughout most of the world, and we are investigating interim mechanisms to involve as many scientists as possible who wish to participate but currently cannot access this site.

We sincerely hope that you will join this global initiative. If we can achieve a greater level of communication, coordination, and multidisciplinary collaboration in the areas of malaria research and control, the result will be a livelier, richer, and more productive field for us all.

Sincerely,

Carole A. Long, Ph.D.
John W. Barnwell, MPH, Ph.D.
Dyann F. Wirth, Ph.D.
Mary R. Galinski, Ph.D.
Robert H. Nagel, Ph.D.

Drs. Carole Long, John Barnwell, Mary Galinski, and Dyann Wirth are all researchers in the area of malaria and are the founding members of the MRN. Dr. Robert Nagel holds a doctoral degree in Neurophysiology and has been a pioneer in the development of large-scale computer information systems for both private industry and government agencies. He developed techniques central to packet switching telecommunications networks, made major contributions to the designs of ARPANET, Telenet, and the NASDAQ system, and was instrumental in the creation of the Reuters world-wide computer network for financial information, the first electronic election reporting system for CBS, and air traffic control systems for commercial airspace, and is the holder of 11 patent awards. Dr. Nagel has created the MRN database design and will be its technical director.

Malaria Genome Focus Group Working Document

This DRAFT Working Document has resulted from a Focus Group Meeting that was sponsored by the Burroughs Wellcome Fund and convened by the Malaria Foundation in Rockville, Maryland, USA on April 7th 1997. This document will be revised beginning mid June to accommodate the views of the broader scientific community.

It is crucial that you review this Working Document and forward your comments by e-mail to MalariaGenome@Malaria.org. With your feedback, the Final Document, resulting from this effort, will better represent the views of the malaria research community at large. When responding, please indicate which section of the document you are commenting on.

Even if you generally agree with the content of this document as it currently stands, and have no comments at this time, please take a moment to let us know this, that you are interested in this discussion, and if you would like to receive a copy of the Final Document once it is completed sometime in July. Please send a few words along these lines to MalariaGenome@Malaria.org.

Many thanks in advance for your time and effort towards the successful development of this document! We look forward to hearing from you.

Malaria Genome Focus Group Working Document

To download this file in Microsoft Word format, click here

Introduction: Current malaria genome project and update on progress

Recognizing the recent advances that have been made in high throughput sequencing of DNA and in bioinformatics and especially their application to sequencing the genomes of bacterial pathogens, a number of investigators considered, in late 1995/early 1996, undertaking the complete sequencing of the genome of *Plasmodium falciparum*. Given the potential benefits of this project, several funding agencies expressed an interest in providing support and collaborating on this project. A meeting, co-organized by the National Institute of Allergy and Infectious Diseases (NIAID) and the Burroughs Wellcome Fund (BWF), was held in May 1996 to coordinate the activities of the various funding agencies. In addition to NIAID and BWF, representatives from the Department of Defense (DoD) and the Wellcome Trust (WT) participated in the

meeting. At that meeting, the various organizations agreed to coordinate their activities and announced the following:

- All sequencing groups agreed to work on the 3D7 strain of *P. falciparum*.

- The WT announced that it would support the Sanger Centre with malaria expertise provided by investigators at Oxford University.

- The NIAID announced that it would support, with funds from the NIH Office of Research on Minority Health, sequencing efforts at the The Institute for Genomic Research (TIGR) in collaboration with Naval Medical Research Institute (NMRI).

- The BWF agreed to provide support for pilot projects which would address some of the technical hurdles involved in handling and sequencing *P. falciparum* DNA.

- The DoD representatives agreed to go forward with a proposal to DoD for support of the project.

In December 1996, a meeting, again co-organized by NIAID and the BWF, was held in Baltimore, MD. The meeting brought together representatives from the sequencing centers (NMRI/TIGR and Oxford/Sanger), from the pilot projects and from the funding agencies. In addition, there was participation of investigators involved in the *P. falciparum* chromosome mapping project and the EST/GST projects.

Efforts have been underway for several years to provide maps of the *P. falciparum* chromosomes. Status of that project can be found on the Internet at http://www.wehi.edu.au/biology/malaria/genomeInfo/MapData/MapData.html>. The sequencing of Expressed Sequence Tags (ESTs) of cDNAs from blood stage parasites and Genome Sequence Tags (GSTs) of a mung bean nuclease library has been undertaken by John Dame and collaborators at the University of Florida. The goal of this project is to identify approximately 75% of *P. falciparum* genes. At present, the project has sequenced approximately 3,000 tags. Details of the status of this project can be found on the Internet at <http://parasite.arf.ufl.edu/malaria.html>.

As a result of the discussions and review of progress made, the investigators and funding agencies agreed, at the December meeting, on the following:

- Increased effort should be given to shotgun sequencing of isolated whole chromosomes. Sanger Centre will complete chromosome 3, and TIGR was to initiate sequencing of chromosome 2. Since that meeting, these sequencing centers and a group at Stanford have agreed upon dividing the remaining chromosomes among themselves. Results of initial chromosome 3 shotgun sequencing efforts can be accessed on the Internet at <http://www.sanger.ac.uk/pathogens/>.

- The groups involved in the sequencing project should meet again in June, 1997 to review progress. A meeting has now been scheduled for June 16-17 at the Sanger Centre.

- Effort should continue on projects to facilitate the full-scale cloning effort, including generation of large insert libraries, overcoming clonal instability, gap closure, etc.

-

Discussion should be held within the broader malaria community on additional malaria genome projects which would advance research and would lead to development of diagnostics, drugs and vaccines. Issues under consideration included which other malaria species (*P. vivax* and/or rodent malaria, other) should be sequenced either as full-scale sequencing or more limited EST or GST projects; also, are there other projects which would complement the large-scale sequencing effort underway for *P. falciparum*?

- Also under consideration were plans to begin to think ahead about ways to capitalize on the genome information; e.g. comparative genomics, whole genome approaches to functional analysis.

- Thought should be given to mechanisms by which the information derived from the genome project would be made available to the entire malaria community in a manner that would promote its optimal utilization.

It is these last three points that formed the impetus for the Malaria Genome Focus Group Meeting and subsequent discussions in the malaria research community.

At the request of the Burroughs Wellcome Fund, the Malaria Foundation convened the Malaria Genome Focus Group, which was held on April 7, 1997 in Rockville, Maryland, USA. This group (*participants listed below*) came to a general consensus on the following points which were up for discussion.

It is now crucial that you review this Working Document and forward your comments by e-mail to MalariaGenome@Malaria.org. With your feedback, the final document, resulting from this effort, will better represent the views of the malaria research community at large. When responding, please indicate which section of the document you are commenting on. *Many thanks in advance for your time and effort!*

The URL links mentioned above and others can be found at the Malaria Foundation's web page designated "For the Scientific Community," <http://www.malaria.org/SCICOMM.HTM>. Please also note that a list of reading material relevant to malaria genome projects is being compiled for presentation at this site. *Suggestions for this reading list are also welcome*.

POINTS for DISCUSSION

A. How can the sharing of information and resources relevant to malaria genome research be improved?

- **1.** Networking is crucial for the success of the overall malaria genome project.

  2. Networking will involve the sharing of information as well as the sharing of resources and will help to involve a larger community of scientists in malaria genome initiatives.

  3. The malaria genome project will provide a platform from which new approaches to this problem can be pursued and public awareness of malaria can be enhanced.

  4. The scientific community can pro-actively aid this process, which ultimately could lead to greater resources and productivity towards the development of malaria drugs, diagnostics, and vaccines.

5. Importantly, effective networking will also help to attract investigators from other specific disciplines, such as biochemistry, cell biology, or immunology, to malaria research.

B. What are key biological questions that can be addressed once *Plasmodium* genomic DNA sequence is in-hand?

- **1.** What are the complete biochemical pathways present in malaria parasites? Which of these may be targets for future drug development? What can the biochemical pathways tell us about the biology of these organisms?

  2. What parasite gene products modulate host responses, and what are the genetic determinants for virulence and pathogenesis? What parasite gene products are obvious targets for vaccine development (e.g. surface proteins, enzymes etc.)?

  3. How are malaria parasite organelles unique, and what are their functions?

  4. What can we learn from comparative genomics; i.e. comparison of malaria genome data with genome information of other organisms?

  5. What are the mechanisms of Plasmodium's genetic diversity, including antigenic variation, drug resistance, evolutionary diversity, and mutation frequency?

  6. How does *Plasmodium* genetic diversity influence the epidemiology of disease, and how can we more effectively approach this question with new genomic information? How can this information be utilized to develop more specific diagnostic tools or malaria vaccines?

  7. What are the determinants of sexual differentiation, stage-specific expression, and differential expression in response to environmental stimuli?

C. Should the genome(s) of other *Plasmodium* species be sequenced in parallel (i.e., in addition to *P. falciparum*)? If so, which genome(s)? Also, should the approach for other species be whole genome sequencing or EST/GST sequencing?

- **1.** Additional malaria genome information from other species of *Plasmodium* would be valuable to the scientific community, both for understanding key biological features of malaria parasites, and for the development of malaria drugs, diagnostics, and vaccines. Moreover, genome information from other malaria species provides the basis for the use of model test systems and an important level of comparative genomics between highly divergent groups of *Plasmodium* species.

  2. The consensus of this group is that the focus of other efforts should be on *Plasmodium vivax* and on a rodent malaria species.

  3. Many participants considered it important for *P. vivax* to be included in the malaria genome sequencing efforts because 1) it is a major human pathogen, 2) it is evolutionarily distinct from *P. falciparum*, and 3) unlike *P. falciparum*, the DNA of *P. vivax* is of lower overall A/T content and is generally stable in *E. coli*. Acquisition of *P. vivax* DNA for genome work is feasible, as are biological studies, particularly within the framework of network support.

4. Genome sequence information from a rodent malaria species was considered important because 1) such a model system is manipulatable and generally available to large and small laboratory groups, and 2) given the recent successes in genetic transformation of *Plasmodium*, a rodent model system will be especially important for studying the general biology and genetics of malaria parasites. While no conclusions were reached, the majority of the discussion focused on *P. berghei* and *P. yoelii* as candidate rodent genomes, with some inclination towards the former since it can be cultivated in-vitro and has been genetically transformed with success.

5. *P. vivax* and rodent malaria genome sequencing should be carried out in parallel with the *P. falciparum* project, and need not compromise the success of this project. It was generally agreed that the *P. vivax* and rodent malaria genome projects would be greatly facilitated by the development of cost-effective focused research networks, and that, rather than being detrimental to the *P. falciparum* project, would, in fact, provide valuable information to this project.

6. Pilot malaria genome projects on other malaria species should be initiated and supported, with an initial focus on EST/GST sequencing and chromosome mapping, and not necessarily, at this immediate time, on additional whole genome sequencing projects. The EST/GST approach is both low in cost (estimate is ~$10/EST/GST, based on the costs of the *Toxoplasma gondii* project) and will produce valuable data in a short time horizon. The minimal target for these pilot projects should be ~15,000 ESTs/GSTs per genome, based on an estimate of 7,500 genes. This compromise consensus, on an initial focus towards EST/GST sequencing, should not preclude whole genome characterization if scientific and fiscal evaluations indicate such an undertaking(s) is feasible and desirable, particularly in the case of *P. vivax*.

D. What tools/reagents will facilitate full utilization of *Plasmodium* genomic information that is generated? What complementary projects should be initiated now to maximize the use of incoming malaria genome information?

- **1.** Standardization of parasites (i.e., isolates/strains generally used in malaria research laboratories), gene banks, and repositories for selected reagents is required. Malaria research, today and as new sequence information becomes available, would be greatly facilitated by the general availability of high quality and well-characterized genomic DNA and cDNA libraries for both human malaria parasites and selected non-human malaria models. Further, a central reagent repository(ies) could include a variety of tools such as specific monoclonal antibodies and antisera, recombinant proteins, indexed and tagged cloned ESTs and GSTs, YACs, and BACs*, transformation vectors, and standardized parasite strains. Designated facilities for research requiring the use of specialized animal models or insect stages would also provide valuable complementary support if made generally available and accessible.

2. Comments are specifically requested to learn what malaria researchers in the broad scientific community might like to see available in repositories. Please prioritize your suggestions. Also, what special resources or networks would be especially useful to this field?

3. The well-recognized, generally high instability of *P. falciparum* DNA sequences in *E. coli*, as well as the presence of frequent very long stretches of A or T sequences, are likely to be significant problems in the derivation of the complete and accurate *P. falciparum* genomic sequence. Hence, it is recommended that a systematic effort be undertaken to explore various strategies to overcome this

problem. These could include identifying alternative host-vector systems, or identifying *E. coli* mutants in which large fragments of *P. falciparum* DNA can be stably maintained.

4. One immediate application of sequence information will be in the area of molecular genetic analysis. Several necessary molecular tools now exist, but improvements in their application and efficiency of use are of high priority.

- **a.** Basic genetic manipulation of malaria parasites should be further developed and improved. This will require the identification and utilization of additional selectable markers, the enhancement of transfection efficiency, as well as the identification of promoter/regulatory regions for differential and stage-specific expression.

  b. Complementation analysis capabilities should be developed, which could include the use of heterologous systems such as yeast and *Toxoplasma gondii*, as well as the malaria parasite itself. This will be facilitated by the identification of centromeres for chromosomal complementation and the development of *Plasmodium* artificial chromosomes.

  c. Information and materials from currently recorded laboratory genetic crosses is extremely valuable and should be made generally available to the malaria research community. The development and analysis of additional laboratory genetic crosses, as well as studies aimed at comparatively analyzing natural crosses, should also be given consideration.

  d. Possibilities for developing attenuated parasites should be explored.

5. Culture Technology should be expanded to include the further development of

- **a.** *P. falciparum* exoerythrocytic culture systems, in-vitro and in-vivo, such as in SCID mice;

  b. culture systems for other *Plasmodium* species and stages of the life cycle; and

  c. *P. falciparum* axenic culturing systems.

6. Whole Genome Expression Screening Technologies should be developed for *Plasmodium*.

- **a.** The latest technologies for utilizing the DNA sequence information of entire genomes to best understand the complex phenotypes of the corresponding organisms should be explored. In particular, the recently developed “DNA chip technology” should be investigated for applications in malaria research.

  b. Technological advances in expression screening could also aid efforts to assess differential expression, for example, due to environmental stimuli or *var* gene switching.

  c. Expression screening advances could also have especially important applications in the area of malaria diagnostics

7. Homology Cloning projects could be valuable for obtaining and studying selected genes from other *Plasmodium* species.

* YACs = Yeast Artificial Chromosome
  BACs = Bacterial Artificial Chromosomes

E. What is the best way to facilitate access to information generated in malaria genome projects for the broader scientific community? How can the current databases be linked and the information be shared in a common format?

- **1.** It was a general consensus of the meeting that there was an immediate need to facilitate the sharing of available *Plasmodium* genomic sequence information, and to make these data available and understandable to the widest possible scientific community.

  2. A central and coordinated site for *Plasmodium* genome sequence information should be established and maintained. It is recommended that this site be located in one of the major genome reference centers, such as Genbank, and that a dedicated staff member be employed to facilitate access to and the coordination of malaria genome information.

  - **a.** This site should be user friendly and include educational tools for the user, with access to any necessary training at the site.

    b. This site should also have a variety of relevant searching options.

    c. This site should contain an ORF database, catalogued EST and GST information, chromosomal maps, contig maps, and data from genetic crosses concerning inheritance, among other relevant information.

  3. Both finished and unfinished sequence should be collected and made available at this site. Immediate release of sequence information is strongly supported. Notwithstanding, investigators should be made aware of potential pitfalls in working with immediate-release sequence information. Sequence releases should include trace information.

  4. The current information from the YAC based mapping of *P. falciparum* chromosomes should be collated and made generally available to the scientific community as rapidly as possible. Efforts should also be made to start placing available ESTs and GSTs, as well as microsatellite markers on these maps, also within a short time frame. This data will likely be important for the whole genome sequencing of *P. falciparum*.

  5. It was also suggested that a common interface be developed so that a variety of databases and search engines could be easily interrelated.

F. How can comparative genomic approaches facilitate our understanding of malaria genome information? How can "genomics" be used to obtain information beyond that which can be obtained from "pre-genomic" approaches?

- **1.** Genomics as a science is relatively new and there is clearly a lot to be learned from the many genome projects being conducted today, which could assist investigators in understanding the information contained in malaria genomes.

  2. Information from malaria genome project efforts should be linked with information derived from other microbial genome projects. These links should be made to the public sector and to the private or industrial sector.

3. Available information from both the human host and parasite genomes should be easily comparable to facilitate understanding of the nature of the human host-parasite relationships.

4. Information from malaria vector genome projects should also be integrated as it becomes available.

Remember...
This document will be revised beginning mid June to accommodate the views of the broader scientific community.

 ***Be sure your views are heard! It is crucial that we obtain feedback NOW from as many malaria research scientists as possible. General and specific comments are welcome in response to the Discussion Points listed above.***

Even if you generally agree with the content of this document as it currently stands, and have no comments at this time, please take a moment to let us know this, that you are interested in this discussion, and if you would like to receive a copy of the Final Document once it is completed sometime in July. *Thank you very much.*

All comments should be sent by e-mail to MalariaGenome@malaria.org.

Malaria Genome Focus Group

Co-Organizers:

Enriqueta C. Bond, Martha G. Peck, Jennifer Russo Wortman, Stephanie L. James, Michael Gottlieb, Carole A. Long, Dyann F. Wirth and Mary R. Galinski.

Participants at the April 7th Meeting:

Ripley Ballou, John W. Barnwell, John B. Dame, Mary R. Galinski, Michael Gottlieb, Mark S. Guyer, Stephen L. Hoffman, Stephanie L. James, Altaf A. Lal, Michael Lanzer, Carole A. Long, Wilbur K. Milhous, Robert H. Nagel, Kathryn Nason-Burchenal, Pradip Rathod, Jennifer Russo Wortman, Akhil B. Vaidya, Sara Volkman, Richard Warren, Andrew P. Waters, Tom E. Wellems, and Dyann F. Wirth (Chair).

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