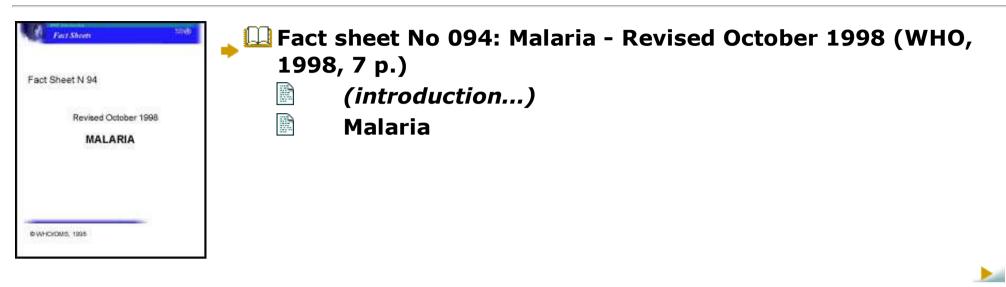
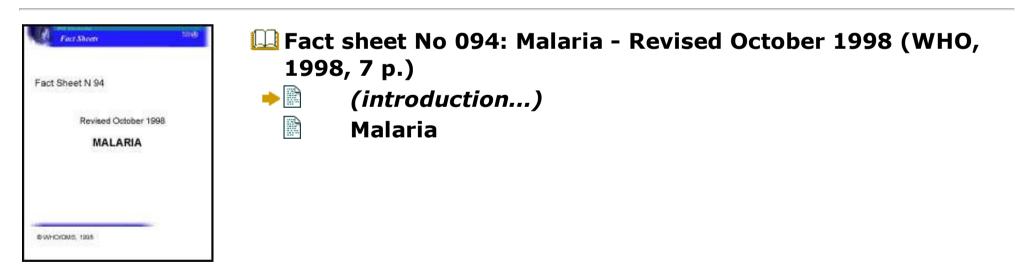
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(introduction...)



Malaria

Malaria is by far the world's most important tropical parasitic disease, and kills more people than any other communicable disease except tuberculosis. In many developing countries, and in Africa especially, malaria exacts an enormous toll in lives, in medical costs, and in days of labour lost. The causative agents in humans are four species of *Plasmodium* protozoa (single-celled parasites) - *P. falciparum*, *P. vivax*, *P. ovale* and *P. malariae*. Of these, *P. falciparum* accounts for the majority of infections and is the most lethal. Malaria is a curable disease if promptly diagnosed and adequately treated.

Prevalence

The geographical area affected by malaria has shrunk considerably over the past 50 years, but control is becoming more difficult and gains are being eroded. Increased risk of the disease is linked with changes in land use linked to activities like road building, mining, logging and agricultural and irrigation projects, particularly in "frontier" areas like the Amazon and in South-East Asia. Other causes of its spread include global climatic change, disintegration of health services, armed conflicts and mass movements of refugees. The emergence of multi-drug resistant strains of parasite is also exacerbating the situation. Via the explosion of easy international travel, imported cases of malaria are now more frequently registered in developed countries. Malaria is re-emerging in areas where it was previously under control or eradicated e.g., in the Central Asian Republics of Tajikistan and Azerbaijan, and in Korea.

The current global picture:

- Malaria is a public health problem today in more than 90 countries, inhabited by a total of some 2 400 million people - 40% of the world's population.
- Worldwide prevalence of the disease is estimated to be in the order of 300-500 million clinical cases each year.
- More than 90% of all malaria cases are in sub-Saharan Africa.
- Mortality due to malaria is estimated to be over 1 million deaths each year. The vast majority of deaths occur among young children in Africa, especially in remote rural areas with poor access to health services.

 Other high-risk groups are women during pregnancy, and non-immune travellers, refugees, displaced persons and labourers entering endemic areas.

• Malaria epidemics related to political upheavals, economic difficulties and environmental problems also contribute in the most dramatic way to death tolls and human suffering.

• Malaria is endemic in a total of 101 countries and territories: 45 countries in WHO's African Region, 21 in WHO's Americas Region, 4 in WHO's European region, 14 in WHO's Eastern Mediterranean Region, 8 in WHO's South-East Asia Region, and 9 in WHO's Western Pacific Region.

Symptoms

Symptoms of malaria include fever, shivering, pain in the joints, headache, repeated vomiting, generalized convulsions and coma. Severe anaemia (exacerbated by malaria) is often the attributable cause of death in areas with intense malaria transmission. If not treated, the disease, particularly that caused by *P. falciparum*, progresses to severe malaria. Severe malaria is associated with death.

Transmission

Malaria is transmitted by Anopheline mosquitoes, the number and type of which determine the extent of transmission in a given area. Transmission of malaria is affected by climate and geography, and often coincides with the rainy season.

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Communities Affected

More than any other disease, malaria hits the poor. Malaria endemic countries are some of the world's poorest. Costs to countries include costs for control and lost workdays - estimated to be 1-5% of GPD in Africa. For the individual, costs include the price of treatment and prevention, and lost income.

Rural communities are particularly affected. In rural areas, the rainy season is often a time of intense agricultural activity, when poor families earn most of their annual income. Malaria can make these families even poorer. In children, malaria leads to chronic school absenteeism and there can be impairment of learning ability. Urban malaria is increasing due to unplanned development around large cities, particularly in Africa and South Asia.

Malaria and Children

Malaria kills one child every 30 seconds. This preventable disease has reached epidemic proportions in many regions of the world, and continues to spread unchecked.

In absolute numbers, malaria kills 3 000 children per day under five years of age. It is a death toll that far exceeds the mortality rate from AIDS.

African children under five years of age are chronic victims of malaria, suffering an average of six bouts a year. Fatally-afflicted children often die less than 72 hours after developing symptoms. In those children who survive, malaria also drains vital nutrients from children, impairing their physical and intellectual development. Malarial sickness is also one of the principal reasons for poor school

attendance.

Yet protection of children can often be easy. Randomised control trials conducted in the Gambia, Ghana, Kenya and Burkina Faso, for example, show that about 30 per cent of child deaths could be avoided if children slept under bednets regularly treated with recommended insecticides such as pyrethroids. Unlike early insecticides such as DDT, pyrethroids are derived from a naturally occurring substance, PYRETHRUM, which is found in chrysanthemums and will remain effective for 6 to 12 months.

Malaria is also particularly dangerous during pregnancy. It causes severe anaemia, and is a major factor contributing to maternal deaths in malaria endemic regions. Pregnant mothers who have malaria and are HIV-positive are more likely to pass on their HIV status to their unborn child.

UNICEF recognises that malaria is one of the five major causes of under-five child mortality. The agency has made the disease a top priority, supporting malaria control programmes in 32 countries, 27 of which are in Africa.

Economic Costs

The estimated costs of malaria, in terms of strains on the health systems and economic activity lost, are enormous. In affected countries, as many as 3 in 10 hospital beds are occupied by victims of malaria. In Africa, where malaria reaches a peak at harvest time and hits young adults especially hard, a single bout of the disease costs an estimated equivalent of 10 working days.

Research indicates that affected families clear only 40 per cent of land for crops D:/cd3wddvd/NoExe/Master/dvd001/.../meister10.htm compared with healthy families. Knowledge about malaria is markedly low among affected populations. In one recent survey in Ghana, for example, half the respondents did not know that mosquitoes transmit malaria.

The direct and indirect costs of malaria in sub-Saharan Africa exceed \$2 billion, according to 1997 estimates.

According to UNICEF, the average cost for each nation in Africa to implement malaria control programmes is estimated to be at least \$300,000 a year. This amounts to about six US cents (\$.06) per person for a country of 5 million people.

Malaria's reach is spreading

In malaria endemic parts of the world, a change in risk of malaria can be the unintended result of economic activity or agricultural policy that changes the use of land (e.g. creation of dams, irrigation schemes, commercial tree cropping and deforestation).

"Global warming" and other climatic events such as "El Nio" also play their role in increasing risk of disease. The disease has now spread to highland areas of Africa, for example, while El Nio events have an impact on malaria because the associated weather disturbances influence vector breeding sites, and hence transmission of the disease. Many areas have experienced dramatic increases in the incidence of malaria during extreme weather events correlated to El Nio. Moreover, outbreaks may not only be larger, but more severe, as populations affected may not have high levels of immunity. Quantitative leaps in malaria incidence coincident with ENSO (El Nio/Southern Oscillation) events have been recorded around the world: in Bolivia, Columbia, Ecuador, Peru and Venezuela in South America, in Rwanda in Africa, and in Pakistan and Sri Lanka in Asia.

In today's international world, the phenomenon of "airport malaria", or the importing of malaria by international travellers, is becoming commonplace. The United Kingdom, for example, registered 2364 cases of malaria in 1997, all of them imported by travellers. 'Weekend malaria', which happens when city dwellers in Africa return to their rural settings, is becoming an increasing problem.

Prevention and cure

Prevention of malaria encompasses a variety of measures that may protect against infection or against the development of disease in infected individuals. Measures that protect against infection are directed against the mosquito vector. These can be personal (individual or household) protection measures e.g., protective clothing, repellents, bednets, or community/population protection measures e.g., use of insecticides or environmental management to control transmission. Measures which protect against disease but not against infection include chemoprophylaxis.

In spite of drug resistance, malaria is a curable disease, not an inevitable burden. Although there is only a limited number of drugs, if these are used properly and targeted to those at greatest risk, malaria disease and deaths can be reduced, as has been shown in many countries.

Disease management through early diagnosis and prompt treatment is fundamental to malaria control. It is a basic right of affected populations and

needs to be available wherever malaria occurs. Children and pregnant women, on whom malaria has its greatest impact in most parts of the world, are especially important.

In many countries, most cases of malaria are diagnosed and treated in the home or by private sector practitioners, often incompletely and with irrational regimens. This speeds up the spread of parasite resistance to antimalarial drugs, which poses another problem - a dramatic rise in the cost of treating uncomplicated malaria (which has been seen in some parts of the world).

Whereas formerly malaria control depended on insecticide spraying, now the selective use of protection methods, including vector control, is proving cost-effective and more sustainable. So, whereas house-spraying is now restricted to specific high-risk and epidemic-prone areas, increasing use is being made of insecticide-treated bednets.

Malaria control is everybody's business and everyone should contribute to it, including community members and people working in education, environment, water supply, sanitation, and community development. It must be an integral part of national health development and community action for control must be sustained and supported by intersectoral collaboration at all levels and by monitoring, training and evaluation, and operational and basic research.

Efforts to Combat Malaria

Global Malaria Control Strategy

Malaria has been a priority for WHO since its founding in 1948. Control activities

are coordinated by WHO's Programme on Communicable Diseases (CDS). The four basic technical elements of WHO's Global Malaria Control Strategy are:

1. Provision of early diagnosis and prompt treatment for the disease;

2. Planning and implementation of selective and sustainable preventive measures, including vector control;

3. Early detection for the prevention or containment of epidemics; and,

4. Strengthening of local research capacities to promote regular assessment of countries' malaria situations, in particular the ecological, social and economic determinants of the disease.

Roll Back Malaria

What has been achieved to date is both a political commitment to malaria control and a progressive strengthening of national and local capacities for assessing malaria situations and selecting appropriate measures aimed at reducing or preventing the disease. National plans of action have also been developed in more than 80% of malaria endemic countries.

Recognizing the widespread political desire that had been building since the Amsterdam Summit of 1992 when the Global Malaria Control Strategy was adopted, Dr Gro Harlem Brundtland, Director-General of World Health Organization, declared upon taking office in July 1998 that there should be a deeper commitment to win the fight against malaria. This was going to require not only the commitment of the health sector, but also other governmental sectors, the private sector where activities may directly or indirectly affect the malaria situation, nongovernmental organizations, and affected communities themselves. Greater financial resources and a higher visibility for malaria campaigns would be necessary. It was thus that, through the offices of WHO, four UN-System agencies (UNDP, UNICEF, WHO and the World Bank) launched *Roll Back Malaria* on 30 October 1998 (see WHO Press Release and WHO Fact Sheet (No 203) on the subject for more details on the project; <u>http://www.who.int/inf</u>).

International Efforts

The Multilateral Initiative on Malaria (MIM) was launched in Dakar in January 1997 when a number of institutions (from both public and private sectors) joined forces to promote malaria research in Africa. The UNDP/World Bank/WHO Special Programme on Tropical Diseases (WHO/TDR) has joined the initiative, establishing a Task Force to address the needs of endemic countries and to fund activities related to strengthening research capacities in malaria; a budget of about US\$3 million a year has been raised, with contributions from several institutions to support research /capacity building projects and training. The Task Force has mobilised around 40 countries and 161 partners for submitting proposals for review. Fifteen partnership projects involving 20 African and 5 European countries and the USA have been funded.

Recent advances in research and development

Field Applications

Significant progress has been made in research on, and development of, new tools

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for use in malaria control activities.

Insecticide treated bednets and curtains have emerged in recent years as a promising tool although their use in Africa is limited. Results from multi-centre randomized, controlled field trials in Africa supported by (TDR) suggest that in certain epidemiological situations, overall childhood mortality can be lowered by 15 to 35% through the use of insecticide-impregnated bednets. Further research is required to enhance the effectiveness of bednets or curtains in operational settings and to ensure their use in a sustainable manner.

Due to the considerable overlap in signs and symptoms of several childhood diseases, a single diagnosis for a sick child is often inappropriate. WHO and UNICEF have responded to this challenge by developing an approach referred to as the "Integrated Management of Childhood Illness". Evidence from surveys of health worker performance and of management of illness in the home suggests that improvements are likely to reduce childhood mortality significantly.

Despite the simple technology and relatively low direct costs, microscope diagnosis is still expensive, requiring an adequate infrastructure to purchase and maintain supplies and equipment, to train health workers and to ensure proper quality assurance of the service. The results of recent evaluations of standardized antigen detection tests including 'dipsticks' suggest that they have potential for use in the management of malaria disease, if accuracy can be assured and the test made affordable for those in need.

New user-friendly packaging of anti-malarials separates the dose to be taken at each time point, and provides simple non-medical information to patients. It can

result in 20% more malaria sufferers following their treatment through until they are cured, and this greater compliance in turn means less possibility of drug resistance developing.

Rectal artesunate is being developed because patients in malaria endemic countries, who are commonly at high risk of death from malaria, often cannot get to health services. So an existing drug is being reformulated for a new indication: emergency treatment to cover a patient on the way to hospital. If regulatory approval is justified, the suppositories will be used for treating severely ill patients who cannot take drugs by mouth and who cannot rapidly access safe injectable treatment.

Drug and Vaccine Development

A limited number of drugs for treatment of malaria are available today. Because of worsening problems of drug resistance in many parts of the world, adequate treatment of malaria is becoming increasingly difficult. Although some new drugs have appeared in the last 20 years (e.g., mefloquine, halofantrine, artemisinin derivatives, malarone, atovaquone + proguanil, co-artemether), new (especially inexpensive and affordable) drugs and more practical formulations of existing drugs/compounds are badly needed.

In Africa, with increasing levels of chloroquine resistance and fears of toxicity and decreased efficacy for sulfadoxine/pyrimithamine, there is an urgent need for an affordable, effective and safe alternative to chloroquine. In the short-term, amodiaquine is being reconsidered as a first or second line drug in areas of chloroquine resistance. There are also studies on the combination of the short

half-life antifolates, chloroproguanil and dapsone, and on pyronaridine, a Chinese synthetic compound. Both are in development by WHO/TDR.

Artemisinin derivatives presently show no cross-resistance with known antimalarials and as such are important for treating severe malaria in areas of multidrug resistance; however, they require long treatment courses and when used alone, recrudescence may occur. TDR has conducted randomised multicentre trials with intramuscular artemether and is currently developing arteether for severe/complicated disease.

Drug combinations for multidrug resistant malaria are being developed by the private sector: atovaquone + proguanil (now registered) and artemether + benflumetol (yet to be registered).

MMV, the new Medicines for Malaria Venture, is a public/private sector initiative to develop anti-malarials and make them available in poor countries. Support for this venture is being solicited from foundations and other public sources as well as the pharmaceutical industry - it could amount to a \$30 million a year programme.

In the last decade, considerable progress has been made in the search for a malaria vaccine. An effective vaccine would constitute a powerful addition to malaria control. More than a dozen candidate vaccines are currently in development, some of them in clinical trial. The hope is that an effective vaccine will be available within the next 7-15 years.

Vaccines for malaria are being developed at global level; clinical trials are ongoing in USA, Colombia, Switzerland, Australia, Papua New Guinea, Gambia and

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Tanzania. The three main types of vaccine being developed are:

"Anti-sporozoite" vaccines, designed to prevent infection.

"Anti-asexual blood stage" vaccines, designed to reduce severe and complicated manifestations of the disease. Such vaccines could lower morbidity and mortality among children under five years of age in Africa, the main risk group, and their development is given priority by WHO. Several such vaccine candidates are currently undergoing clinical and field testing.

"Transmission-blocking" vaccines, designed to arrest the development of the parasite in the mosquito, thereby reducing or eliminating transmission of the disease.

A cost effective vaccine must be capable of being incorporated into appropriate health delivery programmes, and to provide sufficient duration of immunity. At present, it is difficult to predict when such a vaccine will become available.

Mapping of the malaria genome is being carried out by a consortium of partners, including United States National Institute of Health, the US Department of Defense, Burroughs-Wellcome Fund and the Wellcome Trust. Knowledge of the genome will open the door to more rational ways of discovering new vaccines and drugs.

Another initiative is seeking ways to inhibit the parasite's travelling from the gut of the mosquito to the saliva, where it becomes infective to man.

For further information, journalists can contact Health Communications and Public Relations, WHO, Geneva. Telephone (41 22) 791 2584. Fax (41 22) 791 4858. Email: <u>info@who.ch</u>.

All WHO Press Releases, Fact Sheets and Features as well as other information on this subject can be obtained on Internet on the WHO home page http://www.who.ch/

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