

Human communicable diseases

The rising incidence of malaria and tuberculosis in sub-Saharan Africa is causing great hardship, not only to the individuals affected but also to the economies of the countries where they are rife. Both diseases are becoming more resistant to the drugs that are currently available for treatment and drug resistant strains are posing a global threat.

The International Atomic Energy Agency (IAEA) is responding by sponsoring a programme to build technical competency in molecular and radioisotope-based techniques.

Tuberculosis

In sub-Saharan Africa:

- TB infection rate now exceeds 100/100,000 inhabitants per annum;
- 1.5 million new cases of TB are recorded each year;
- TB causes 600,000 deaths each year, about a quarter of all avoidable deaths;
- It is the leading cause of deaths among adolescents and adults.

Globally:

- TB is likely to kill 30 million people this decade.

Malaria

In sub-Saharan Africa:

- 90% of all malaria cases occur in Africa;
- About 1.8 million people die of malaria each year;
- About 1.6 million children die of malaria each year;
- Malaria accounts for one in five of all childhood deaths;

Globally:

- Approximately 300 million of the world's population suffer from malaria. This is the largest disease burden in the world.

Economic impact

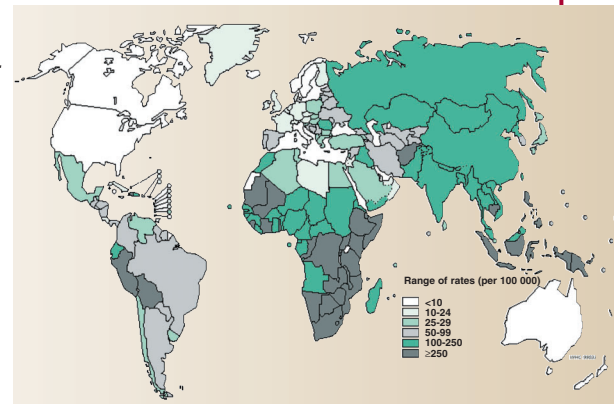
Malaria and TB present a major barrier to poverty eradication in Africa. It has been estimated that malaria alone costs Africa more than US\$ 12 billion annually and slows economic growth on the continent by up to 1.3% each year. The economic impact is felt disproportionately by poor families which spend about 25% of their annual income on malaria prevention and control. TB, especially when associated with AIDS, accounts for US\$ 11 billion in future lost income. It affects what should be the most productive age group in society, effectively impoverishing both households and the nation.

The WHO's approach to controlling the spread of TB focuses on treating those who are infected with effective drug combinations under supervision. The Directly Observed Treatment Short-course, known as DOTS, ensures that the full course of treatment is given.

Photo credit to come



An estimate of the incidence of TB worldwide.



Drug resistance

Both diseases are becoming more difficult and more expensive to cure because resistance to the most widely available drugs is increasing. The mycobacteria (*Mycobacterium tuberculosis*) which cause TB are spread in air-borne droplets and the nature of the disease is such that a person may be infected for many weeks before the symptoms become apparent. And, when they do and treatment is sought, it may not always be effective. If left untreated, one person with active TB will infect 10-15 people in a year's time. In low and middle-income countries, diagnosis of new TB patients has not included testing for drug susceptibility and many cases of primary drug resistant TB have therefore been missed. Many of the strains of mycobacteria that cause TB are now resistant to the three most commonly used anti-TB drugs; rifampicin, streptomycin and isoniazid. This means not only that the individuals affected continue to suffer but also that they will continue to pass on the drug-resistant strains of mycobacteria to other people. It is essential that health authorities are able to detect such strains with the minimum of delay, not least because it costs up to 100 times as much, and takes four times as long, to cure multi-drug resistant TB. The sooner such strains are detected, the quicker the individuals can be properly treated and, overall, fewer people become infected.

Malaria is caused by a parasite that is transmitted to humans through the bite of a female *Anopheles* mosquito. There are four species of the malarial parasite; the most serious illness being caused by the parasite *Plasmodium falciparum*. Mosquitoes have become resistant to many kinds of insecticides, which makes eradication programmes prohibitively expensive for many countries and, in some regions, the parasites have also developed drug resistance.

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The inexpensive anti-malarial drug chloroquine is no longer effective against many parasites necessitating treatment by more expensive drugs and adding to the national cost of disease control. Because malarial parasites are constantly evolving and acquiring more resistance to available drugs, routine surveillance for drug resistance is an essential activity for all malaria control programmes. This is particularly important because the development of new anti-malarial drugs has not been a priority for the pharmaceutical industry.

Detecting resistance

Conventional methods for detecting drug resistance are slow; typically four weeks for malaria and even longer for TB which requires culture (four to six weeks) followed by the determination of drug susceptibility (a further one to two weeks). However recent developments in the field of molecular genetics have led to the identification of genetic mutations that result in drug resistance. Multiple drug resistance is the

consequence of an accumulation of mutations in these genes. The mutations can be identified by molecular methods and used to predict drug resistance in a matter of days. Furthermore, these methods are far more sensitive and allow hundreds of samples to be

Blood films showing P. falciparum infected red blood cells. A normal red blood cell and one in which the malaria parasite is visible.

analysed simultaneously.

The technique used is called PCR (polymerase chain reaction) dot blot hybridization (see box). Most importantly it provides an effective means of surveillance for drug resistance but it also:

- indicates where alternative drugs are likely to be more effective for treating the individual patient;

PCR Dot Blot

PCR-based dot blot hybridization uses DNA extracted from the pathogen to be identified and then amplifies it using the polymerase chain reaction. The amplified DNA is directly "dotted" onto a nylon membrane. Next, radioactively labelled DNA probes, specific to the pathogen's DNA, are added. The membrane is then exposed to Xray film. Spots on the Xray film will appear only when the pathogen has first been bound to the nylon membrane and the radioactively labelled probe has then been bound to the pathogen.

- helps authorities target resources to prevent the transmission of drug resistant TB;
- offers precise and large scale methods to diagnose whether parasites that follow drug treatment for malaria are due to re-infection or resistance.

Technical Co-operation

Since 1997, the IAEA has been supporting national health centres' capability for diagnosis of drug resistance in malaria and TB in seven African countries: Kenya, Mali, Sudan, South Africa, the United Republic of Tanzania, Zambia and Zimbabwe. The programme's scope was expanded under the 2001-2002 technical co-operation biennium to include 11 beneficiary countries and aims at validating the use of isotope and molecular techniques as new diagnostic tools in national disease control and surveillance programmes.

The ultimate goal is to integrate these techniques as advanced decision-making tools within the protocols of national control programmes for malaria and TB.

DNA Fingerprinting

Another nuclear technique, which uses the distinctive DNA pattern or 'fingerprint' of each strain of the tuberculosis mycobacteria, also has clear benefits in the control of multi-drug resistant TB. This is because the same source of infection leaves one kind of fingerprint. For example, if there is a predominance of one fingerprint over a large geographical area, or across different risk groups, this indicates the presence of highly transmissible strains. Health authorities can gain valuable information about the type and pattern of spread of any particular strain and target scarce resources to those situations where the problem is most serious.

International collaboration

The IAEA, which has special expertise in the application of nuclear techniques to medicine, is collaborating closely with the relevant authorities in Member States and with the World Health Organization.

The success of these global initiatives will depend, to a large extent, upon precise and rapid surveillance for drug resistance without which control efforts will be ineffective. Drug resistant TB has developed largely where TB control authorities have poorly implemented the DOTS (Directly Observed Therapy, Short-course) strategy. According to the WHO, there is no cure for some of the known multi-drug resistant strains. There is a real danger that without new intervention and control strategies conventional drugs will become useless. Multi-drug resistant TB and malaria are global problems and no country is immune.

By building capacity in molecular methods of detection, the IAEA is strengthening Member States' decision-making tools in the management of malaria and TB.

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