

Malaria – A Disease that Refuses to Die but Continues to Kill

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Previously an endemic area for malaria, Israel was declared malaria free about 50 years ago. The same holds true for other western countries, including those in the northern hemisphere, almost all having been endemic areas of malaria and that succeeded in eradicating the disease in the 20th century. Yet, today, these countries are encountering an increasing number of imported malaria cases due to extensive travel and migration. Most of the cases seen in western countries are people coming from sub-Saharan Africa – where malaria is the predominant disease.

The most prevalent species of malaria in sub-Saharan Africa is *Plasmodium falciparum*, the lethal malaria pathogen. Each year there are about 2 million cases of death in Africa due to falciparum malaria, usually among children who lack immunity. The other common species of malaria, vivax malaria, can cause significant morbidity but rarely causes severe or lethal disease; however, prevention of vivax malaria is much more complicated [1].

The number of imported malaria cases is alarming. In Europe there are about 7,000–8,000 reported cases annually, but the true estimation is 30,000 cases annually [2]. In the United States there are about 1,400 reported cases annually [3], and in Israel there are 60–100 imported cases annually [4].

Among falciparum malaria cases, about 10% will be severe, and among these, 20% will likely be fatal. In the industrialized countries, including Israel, cases of mortality from malaria occur every year, despite the fact that falciparum malaria can be prevented. Moreover, timely diagnosis and treatment can prevent complications and mortality.

In this issue of *IMAJ*, Ben-Ami and colleagues present data on Israeli travelers who acquired malaria in a resort area in Mombassa, Kenya [5]. Their data show that malaria was acquired in Mombassa after less than 2 weeks stay in a good hotel in a coastal resort area, and that the patients were older than the usual travelers to the tropics since the purpose of travel was recreation and leisure rather than an adventure. Ninety percent of the group did not take recommended prophylaxis. This report illustrates several important issues for Israel as well as for the international travel industry. The general perception of the population is that a short stay in a resort hotel is not associated with risk of acquiring malaria. However, it must be stressed that it is not the type of travel but rather the destination that is the risk factor. Malaria is prevalent in all sub-Saharan Africa, including resort areas, capital cities and tourist destinations. To date, malaria control has not met with any success in Africa. The safe places in sub-Saharan Africa are at high altitudes, where the anopheline mosquitoes cannot transmit the

disease (for example, Addis Ababa in Ethiopia, Nairobi in Kenya, Harare in Zimbabwe).

The outcome in this group of patients was disastrous. Of the 29 cases reported, all were hospitalized; 20% were severe and required hospitalization in an intensive care unit, including one fatal case. Mombassa was an attractive site for Israeli travelers, attracting approximately 1,000 Israeli travelers per month, until the terrorist attack against an Israeli-owned hotel in November 2002. The 29 cases reported here occurred during 3 years of this package tours-type activity. Since we do not know how many travelers used prophylaxis, a calculation of the specific attack rate of malaria in this area is unavailable.

This report should be a strong indicator that prophylaxis is necessary when traveling to malaria-endemic areas, regardless of the nature of the trip. Since malaria is a mosquito-borne disease, all travelers – whether businessmen, leisure seekers, or backpackers – must be made aware that the malaria risk is related to the destination rather than the style of the trip. Africa is the continent with the highest rate of malaria and therefore all efforts must be made to convince travelers of the need for prophylaxis, as well as for protective methods such as using repellent after dark and mosquito nets for sleeping.

Malaria chemoprophylaxis has a bad reputation among travelers because of its severe adverse effects, especially neuropsychiatric disorders. However, the introduction of the new antimalarial drug atovaquone-proguanil has changed the situation due to its lower profile of side effects, mainly gastrointestinal discomfort and no neuropsychiatric disorders [6]. Another advantage is that since the drug acts on the liver stage of the malaria cycle, it should be taken during the trip with no need to continue taking it for 1 month after leaving the endemic area, a fact that may increase patient compliance. This drug is very suitable for short trips to malarious areas.

To date there is no law or regulation that obligates travel agents to inform travelers that their destination carries the risk of malaria. As noted in the article by Ben-Ami and team, many travelers believe that a short trip to a holiday resort does not constitute a risk of malaria. Clearly, the health authorities should mandate travel agents to inform travelers that they must seek medical consultation prior to such travel.

The medical community also needs to be educated regarding the disease. Falciparum malaria can be a severe disease with a high mortality, especially among the elderly [7]. Malaria in travelers is first manifest by high fever, often continuous rather than

intermittent. Since the incubation period of falciparum malaria is on average 2 weeks from the time of exposure, any febrile disease that appears after return from travel to Africa must be suspected of being falciparum malaria. If diagnosed and treated in time, malaria can be treated with complete resolution. Delay in diagnosis and treatment is liable to result in severe disease and ultimately death. Indeed, it is worrying that 77% of the malaria cases reported here were examined by primary care physicians who diagnosed viral infection without considering the possibility of malaria in their differential diagnosis or performing a malaria smear. In Israel, we see at least one malaria case a week, which means that it is not a rare disease. It cannot be emphasized enough that medical students, primary care and hospital physicians need to be alert that a febrile disease in a person returning from endemic areas requires a malaria smear.

Severe malaria requires intravenous treatment with quinine or quinidine. A survey that we conducted revealed that 90% of hospitals do not keep this drug in stock, although it is not expensive (about \$30 per full treatment) and has a shelf life of approximately 4 years [8]. Since timely treatment save lives, hospitals should be obliged to keep this drug in stock.

Furthermore, the Ministry of Health should ensure that new drugs be available in Israel for cases in which resistant malaria is imported. The most promising is the group of artesunate-based combinations (based on the Chinese antimalaria drug, artemisinin). These drugs are currently the drugs of choice recommended by the World Health Organization for treatment of malaria in Africa. Drugs of this family are now manufactured also in the west, for example, artemether-lumefantrine (Riamet®, Coartem®, Novartis). This oral drug is well-tolerated, fast-acting and effective and serves primarily to treat uncomplicated falciparum malaria that is resistant to other antimalarials [9]. To date, we have not come across quinine-resistant falciparum, but due to the spread of resistant

falciparum worldwide we must be prepared for this eventuality, and it is therefore crucial that an emergency stock of drugs exists. Malaria is a disease that refuses to die but continues to kill, and we have to be better prepared.

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