

The return of the big three killers

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The 'big three' killer diseases are malaria, human immunodeficiency virus (HIV)/AIDS, and tuberculosis (TB), which probably account together for >6 million deaths per year. In the past 15 years, major sources of funding, including from the UN's Global Fund, have led to significant progress in the fight against each one of these diseases (<http://www.theglobalfund.org/en/>). However, recent reports and data are calling into question an optimism that might have been too premature.

The access to and early use of effective antimalarial treatment—the most effective antimalarial drugs being artemisinin-based combination therapies and the emerging approach of intermittent preventive treatment—have been key elements in the decline in global malaria incidence in the past 10 years [1]. However, the emergence of artemisinin resistance on the Cambodia–Thailand border is of great concern, and represents a major threat in the fight against malaria [2]. In this issue, Wongsrichanalai and Sibley [3] review the background of artemisinin resistance, its situation, especially in the Greater Mekong Sub-region, the difficulties in defining and measuring resistance to artemisinin-based combination therapies, and the efforts needed to control and limit the spread of resistant parasites. The other major issue in the fight against malaria involves antivector procedures such as indoor residual spraying, the use of long-lasting insecticide-treated bed-nets, and the destruction of larval breeding sites. However, the effectiveness of these tools is now being challenged by the emergence and growth of insecticide resistance [4]. *Anopheles* mosquito vectors have an amazing capacity to adapt. They rapidly develop resistance to insecticides. Their behaviour can also change because of our lifestyle changes. In response to the use of mosquito bed-nets during the night, some *Anopheles* mosquitoes change their biting hours, feeding earlier when people are not yet protected by a net. Also, when exposed to insecticides, indoor mosquitoes start changing their behaviour, biting outdoors and sometimes feeding on animals [5]. In this issue, Sokhna *et al.* [6] review factors jeopardizing vector control, including biological resistance to insecticides and behavioural adaptation to the

insecticide-based vector control interventions. Together, these emerging phenomena may compromise malaria control, and the development of new vector control interventions should be considered. In the future, drug and/or insecticide resistance in a context of weakening of malaria control programmes could lead to a dramatic resurgence of malaria globally [7].

Over the past two decades, the re-emergence of TB in industrialized countries has been linked with immigration, and, in sub-Saharan Africa, with the HIV epidemic. Two major threats have emerged, including the potential for *Mycobacterium tuberculosis* Beijing strains, which are now pandemic, to cause outbreaks, and the rise of drug-resistant TB [8]. Basically, these threats are connected, as the Beijing strain family is characterized by its potential to cause epidemics and its association with drug resistance [9]. Several outbreaks of TB caused by *M. tuberculosis* Beijing have been reported in crowded environments, such as homeless shelters and prisons, and, more recently, in two schools in Marseille, France [9], and Milan, Italy [10]. The high level of contagiousness of the source cases is a major issue. The emergence of extensively drug-resistant TB represents a critical challenge to public health authorities globally. It has recently been brought up as a major concern in TB control in South Africa [11]. In Europe, the problem has also emerged in recent years. It has led to public and political issues, as many cases in Europe have been diagnosed in foreign-born patients and/or asylum seekers, coming from central/eastern Europe or Asia [12,13]. In this issue, Borgdorff and Van Soolingen [14] review the molecular epidemiology of TB, which, over the last two decades, has contributed to its study and to an understanding of its re-emergence. In addition, they also examine the role of whole genome sequencing in answering unresolved questions regarding the fight against TB.

Finally, in this issue, Bozicevic *et al.* [15] present the trends of the HIV epidemic in Europe. They describe an increase in the numbers of reported HIV cases in some countries of western, central and, particularly, of eastern Europe, where TB–HIV co-infection is becoming an important issue. Importantly, HIV

transmission in men who have sex with men is increasing in many European countries. This trend has also been reported outside of Europe, such as recently in China [16]. Interestingly, several European countries have described recent increases in the incidence of several sexually transmitted infections, particularly among men who have sex with men [17]. These data raise questions about prevention, and particularly about communication strategies regarding the preventive interventions for HIV. Sexually transmitted bacterial rectal infections are associated with a higher risk of being infected with HIV [18]. Screening for rectal sexually transmitted diseases and targeting populations for risk reduction-specific counselling is critical. Other prevention strategies might also emerge. Also, rectal microbicides, such as antiretroviral gels, also referred to as topical pre-exposure prophylaxis, are being studied and developed to prevent new HIV infections [19].

In conclusion, the fight against the big three killers is still ongoing, and continuing work on implementing new weapons/strategies is critical.

Transparency Declaration

The author declares no conflicts of interest.

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