

How can we 'end malaria for good' if we cannot identify it?

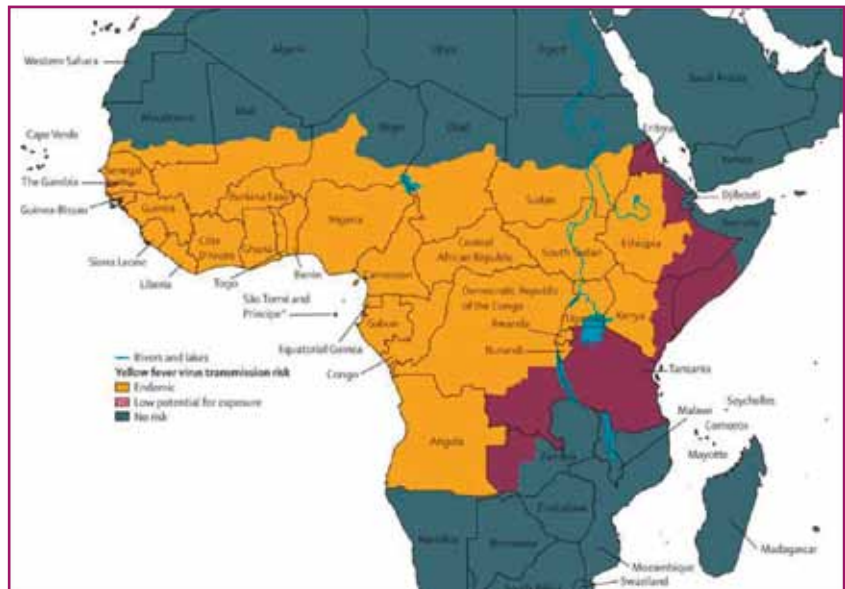
Prof William R Brieger takes issue with the theme for this year's World Malaria Day, pointing out that as things stand, it is simply impractical

The theme for the 2016 World Malaria Day, 'end malaria for good', presents us with a double challenge.¹ We want to end malaria finally, or eliminate it between 2030 and 2040, but also, ending it will be good for saving lives and improving economies of endemic countries. The challenge arises when we consider whether we will have adequate resources to accomplish the task. As colleagues from the University of California in San Francisco observed, 'Sustaining domestic and international funding as malaria burden decreases is a serious concern for most of the eliminating countries'.²

One way to guarantee resources is through conserving what we have and only treating people for malaria when they actually have the disease, and not some other febrile illness. The advent of malaria rapid diagnostic tests (mRDTs) that can be used at the primary care level, including within the community should have improved our ability to differentiate malaria from other causes of fever.³ Unfortunately, mRDTs do not always guide correct case management.⁴⁻⁶ When a febrile patient tests negative, we may not have the ability to do further differential diagnosis. Some causes of fever do not have a direct cure. Therefore if malaria drugs are available through programmes like The Global Fund, we are tempted to use them since many front-line clinicians feel that, 'We must do something for the patient'.

Flaviviruses — a big challenge to correct treatment

Such choices not only waste scarce resources but may be harmful. A prime example is the recent outbreak of yellow fever in Angola.⁷ Unlike malaria, there is currently an effective vaccine for yellow fever. The problem is first in getting adequate supplies in a timely manner and then convincing people to come for the vaccination. In the meantime, people may develop symptoms and



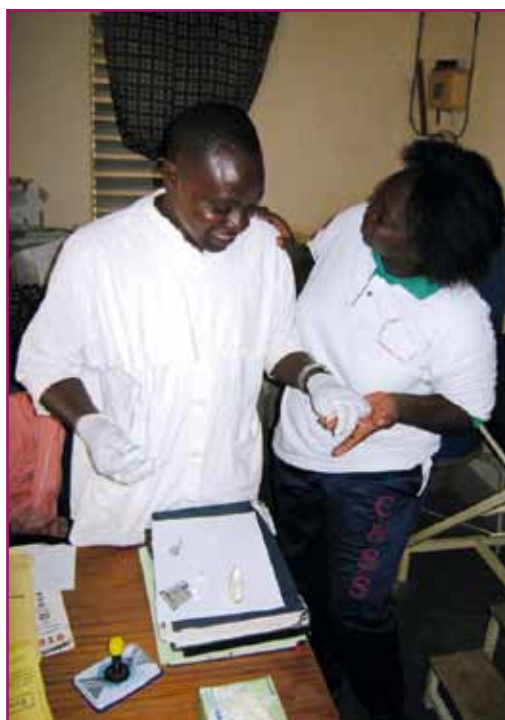
Areas with risk of Yellow Fever virus transmission in Africa. Map is from the following publication: Jentes ES, Pomeroy G, Gershman MD, et al. The revised global yellow fever risk map and recommendations for vaccination, 2010: consensus of the Informal WHO Working Group on Geographic Risk for Yellow Fever. *Lancet Infect Dis* 2011; 11: 622–32.

seek care. According to the World Health Organization (WHO), 'The first, 'acute', phase usually causes fever, muscle pain with prominent backache, headache, shivers, loss of appetite, and nausea or vomiting,' making it easily confused with malaria.⁸ Treating most of these patients with malaria drugs may not cause harm, but 15% go on to develop severe disease including haemorrhaging and death. Proper use of mRDTs, follow-up observation of RDT-negative patients and provision of supportive care that treats dehydration, respiratory failure, and fever, can save lives.

Yellow fever is just one flavivirus, including chikungunya, dengue and Zika, that can frustrate our efforts to focus malaria resources, and at the same time provide quality, appropriate care. For dengue fever, WHO guidance notes that, 'Patients typically develop high-grade fever suddenly. This acute febrile phase usually lasts two to seven days and is often accompanied by facial flushing, skin erythema, generalised body ache, myalgia, arthralgia and headache... Anorexia, nausea and vomiting are common. It can be difficult to distinguish dengue clinically from non-dengue febrile diseases in the early febrile phase'.⁹

RDT kits are widely used in India for the diagnosis of dengue infection,¹⁰ but do not feature in African

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clinics. One possible reason may be the lack of apparent dengue Haemorrhagic Fever (DHF) that arises when all four dengue serotypes are present. A recent study in Burkina Faso confirms the presence of three serotypes.¹¹ Ironically, such documentation of three serotypes in Africa has been available over 45 years based on research in Nigeria.¹² Without dengue RDTs, clinicians in Africa may assume that dengue is a severe form of malaria and treat as malaria even without parasitological laboratory evidence. With suspected dengue patients, increased intake of oral fluids is recommended by WHO along with paracetamol (not aspirin) for fever and pains.

Africa spared worst of Zika so far

So far the global Zika virus outbreak has spared Africa of its worst neurological and brain damaging effects. Ironically, the virus was first identified in Africa, in the Zika Forest between Entebbe and Kampala, in 1947.¹³ Zika was again documented in Nigeria in 1954¹⁴ and

1979¹⁵. The latter Nigerian work explained that Zika-infected persons often present with mild, nondescript illness, including fever, headache, body pains and rash, and so 'it is conceivable that such cases may not report to hospital clinics'.

For the current epidemic the US Centres for Disease Control and Prevention (CDC) inform that, 'The most common symptoms of Zika are fever, rash, joint pain, or conjunctivitis (red eyes). Other common symptoms include muscle pain and headache'.¹⁶ CDC outlines palliative case management, including 1)

Get plenty of rest, 3) Drink fluids to prevent dehydration, 3) Take medicines such as acetaminophen or paracetamol, to relieve fever and pain, and 4) avoid aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs), like ibuprofen and naproxen, until dengue can be ruled out to reduce the risk of haemorrhage.

Like other flaviviruses, chikungunya 'causes fever and severe joint pain. Other symptoms include muscle pain, headache, nausea, fatigue, and rash,' according to WHO.¹⁷ WHO explains that, 'Most patients recover fully, but in some cases joint pain may persist for several months, or even years. Occasional cases of eye, neurological and heart complications have been reported, as well as gastrointestinal complaints'. Appropriate diagnostic tests include enzyme-linked immunosorbent assays (ELISA) and reverse transcriptase-polymerase chain reaction (RT-PCR), but these are not accessible or appropriate for front-line clinics. Therefore clinicians basically need to determine that the symptoms are not

malaria and not dengue. As with the other flavivirus, WHO recommends palliative care with extra fluids and medicine to relieve fever and pains.

And then there is Ebola

The world's largest Ebola outbreak appears to be coming to an end in West Africa. It is important to think back to the initial days when health workers were unfamiliar with this viral haemorrhagic fever and responded to the initial symptoms as if it were malaria. Inability of health workers to initially identify Ebola resulted in their own deaths, fear in the community and a major disruption of standard medical care, including for common and deadly conditions such as malaria.¹⁸ Lacking proper infection prevention materials, health workers were discouraged from using mRDTs.¹⁹

Ebola, a filovirus, can be initially confused with other febrile illnesses. In Sierra Leone, Wen-Gang Li and colleagues screened suspected Ebola cases and found a variety of symptoms including fever, headache, joint pain, fatigue, nausea/vomiting, diarrhoea, and haemorrhage, that were also common in those testing negative for Ebola. The non-Ebola patients were diagnosed with malaria, HIV, Lassa fever, tuberculosis, yellow fever, and pneumonia.²⁰ Health workers who do not have access to diagnostic tests are therefore likely to become infected themselves, as well as miss the underlying disease and be unable to treat the right illness.

When Ebola is prevalent, there are greater risks associated with using mRDTs and possibly spreading Ebola through blood-related procedures. To counteract the threat of malaria it was common in affected countries to engage in mass distribution of anti-malaria medicines without testing. Sierra Leone in late 2014 was reported that, 'More than 9300 trained community health workers went door-to-door in districts where the risk of Ebola is highest to administer anti-malarial tablets to 2.5 million people over three days'.²¹

In conclusion, it will be good to end malaria for good, but only if we also have the means to detect and manage the other dangerous, life-threatening febrile diseases that will be left behind. We should not be continuing to see yellow fever because there is a vaccine, and hopefully dengue will follow suit.^{22,23} In the meantime, we need to conduct proper differential diagnosis, starting with mRDTs so that expensive malaria medicines will be used judiciously and correctly, and other febrile illnesses will receive appropriate life-saving care.

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