Tropical Anemia: One of Africa’s Great Killers and a Rationale for Linking Malaria and Neglected Tropical Disease Control to Achieve a Common Goal

Peter J. Hotez1*, David H. Molyneux2*

1 Department of Microbiology, Immunology, & Tropical Medicine, The George Washington University and Sabin Vaccine Institute, Washington, D. C., United States of America, 2 Liverpool School of Tropical Medicine, Liverpool, United Kingdom

"Wiping out malaria would join the eradication of smallpox as one of the greatest accomplishments in human history. It is a goal we can achieve."

Melinda Gates, co-founder, Bill & Melinda Gates Foundation

With more than 1 million child deaths annually, malaria remains the single leading killer of young children in sub-Saharan Africa [1]. Millions more young children survive, but still suffer from severe anemia and permanent neurological damage [1], as well as more subtle neuropsychiatric disturbances including impaired cognition and memory [2]. Malaria in pregnancy is also a major cause of maternal deaths and low birth weight [3], and together these maternal and child health effects account for huge economic losses that trap families in poverty [4]. As a result, malaria is now considered one of the key forces preventing the development of the African continent [4]. In response to a growing malaria crisis, the Bill & Melinda Gates Foundation recently announced an ambitious program of expanded malaria control, with a long-term goal of malaria eradication [5]. The major elements of expanded malaria control include strengthening of prevention and treatment programs worldwide through the Global Fund to Fight AIDS, Tuberculosis and Malaria, the United States President’s Malaria Initiative, the World Bank Malaria Control Booster Program, scale-up of national control programs [5], coordination through the Roll Back Malaria Partnership based at the World Health Organization (WHO) [6], and advocacy by Malaria No More and other organizations [7].

In the early 1970s, an intensified effort to interrupt the transmission of malaria was conducted in a group of villages near the town of Garki in northern Nigeria [8]. Through household spraying, mass drug administration, and other measures, there was a temporary reduction in malaria deaths, but overall the Garki Project showed that interrupting malaria transmission was not possible even when a full armamentarium of control tools was applied [8]. An important difference between then and now is the availability of long-lasting insecticide-treated nets (LLITNs) and artemisinin combination therapy (ACT)-based treatments, in addition to the increased willingness to deploy indoor insecticide spraying [1]. However, it is unclear whether even the deployment of these new control tools will directly lead to total success in malaria control because of the threat of emerging insecticide resistance to pyrethroids and the potential for emergence of artemisinin resistance [1,9,10]. Also, parallel efforts will be required to strengthen Africa’s weakened health systems [11,12], which today suffer from widespread malaria misdiagnoses in endemic areas [13] and a lack of access to essential medicines and LLITNs [14]. Accordingly, WHO and other organizations are embarking on renewed efforts to strengthen health systems in Africa and elsewhere [15], while product development partnerships have evolved in a concerted push to accelerate the development of additional new malaria drugs and insecticides, and safe and effective anti-malaria vaccines [1,5,16].

There is yet another promising, low-cost and highly cost-effective, and complementary approach for potentially reducing the morbidity of malaria in sub-Saharan Africa, which builds on existing efforts and could be implemented for as little as US$0.50 per person per year or less than 10% add-on to projected malaria control costs [17–20]. In sub-Saharan Africa, where more than 90% of malaria deaths occur, children and pregnant women are simultaneously infected with both malaria and a group of other parasitic diseases, known as the neglected tropical diseases (NTDs). The major NTDs in sub-Saharan Africa include hookworm infection (198 million cases) and other soil-transmitted helminth infections such as ascariasis and trichuriasis (173 million and 162 million cases, respectively), schistosomiasis (166 million), trachoma (33 million), lymphatic filariasis (46 million), and onchocerciasis (18–37 million) [17,18]. There is evidence that some of these NTDs exert an adverse influence on the clinical outcome of malaria in childhood and in pregnancy [21–24], and even possibly on malaria transmission [25]. Shown in Figure 1 is a previously published map demonstrating the geographic overlap and co-endemicity of falciparum malaria and the major NTDs in sub-Saharan Africa [4].


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Peter J. Hotez is Editor-in-Chief of PLoS Neglected Tropical Diseases. He is the Walter G. Ross Professor and Chair of his Department, and President of the Sabin Vaccine Institute. David H. Molyneux is former Director of the Liverpool School of Tropical Medicine and is the Executive Secretary of the Global Alliance to Eliminate Lymphatic Filariasis. He is currently Senior Professorial Fellow at the Liverpool School of Tropical Medicine.

* E-mail: mtmpjhl@gwu.edu or photoez@gwu.edu (PJH); david.molyneux@liverpool.ac.uk (DHM)
hookworm infection (Africa’s most common NTD), based on statistical and spatial analyses [22]. This analysis shows high spatial congruence of these two infections, with one quarter of all sub-Saharan African schoolchildren simultaneously at risk for hookworm and malaria. Almost all of the estimated 50 million schoolchildren in sub-Saharan Africa with hookworm infection are also at high risk for malaria, except in a small band of the Sahel where the climate is presumably too dry to support the larval development of hookworms [22]. A similar association has also been noted between malaria and schistosomiasis [21]. Therefore, early evidence points to high rates of malaria and NTD coinfections in sub-Saharan Africa, especially with hookworm infection and schistosomiasis.

In Africa and other tropical developing countries, the great killer and disabler that results from malaria and NTD coinfections is anemia [23,26–28]. Anemia accounts for up to one half of malaria deaths in young children [26], and is a leading contributor to the huge numbers of maternal deaths that result during pregnancy, as well as premature births [27]. Chronic anemia in young children is also associated with reductions in physical growth, and impaired cognition and school performance [23,24]. Many of the NTDs, but especially two of the most common ones in sub-Saharan Africa, hookworm infection and schistosomiasis, cause anemia [24,28–32], while in Asia (and presumably elsewhere), hookworm infection, schistosomiasis, and trichuriasis result in a synergistic anemia [33]. Malaria also causes severe anemia [26,27], and in cases of malaria and NTD coinfection, anemia in vulnerable children and women develops through one or more of several mechanisms including blood loss, hemolysis, anemia of inflammation, and splenic sequestration [22–24,28–32]. An important consequence of malaria and NTD coinfections is an enhancement in anemia, or what we have called previously “the perfect storm of anemia” [24]. For instance, in Kenya, hemoglobin concentrations were found to be 4.2 g/l lower among children harboring hookworm and malaria coinfections than in children with single-species infections [23]. Because hookworm and schistosomiasis are widespread in Africa [17,21,22], it is likely that these NTDs represent important contributors to the overall mortality from childhood malaria in this region [23,24,28].

![Figure 1. Distribution of Hookworm and Malaria Coinfection.](https://www.plosntds.org/2/July2008/V2/Issue7/e270/figure1.png)
that simultaneously target hookworm and with a rapid-impact package of NTD drugs with anthelminthic drugs ("deworming") or amine or ACT [38] would be supplemented
grams targeted for infants, preschool chil-
and other measures to reduce malaria
control would work in synergy with nets
susceptibility to malaria, so that NTD
reduction, there is also some evidence that
hookworm and schistosomiasis (and possi-
ibly other NTDs) may immunomodulate
their human host and promote increased
susceptibility to malaria, so that NTD
control would work in synergy with nets
and other measures to reduce malaria
incidence [25].

In sub-Saharan Africa, there are several
opportunities to link malaria and NTD
control programs [23]. They include pro-
grams targeted for infants, preschool chil-
dren, or school-aged children that employ
intermittent preventive treatment (IPT), in
which use of either sulfadoxine-pyrimeth-
amine or ACT [38] would be supplemented
with anthelminthic drugs ("deworming") or
with a rapid-impact package of NTD drugs
that simultaneously target hookworm and
other soil-transmitted helminth infections,
lymphatic filariasis, onchocerciasis, and tr-
achoma [17,23,24]. A joint program of malaria and NTD control could be incor-
porated as a new element of Integrated
Management of Childhood Illness and other
programs for children [39]. There are also
opportunities for linking IPT in pregnancy
with anthelminthic drugs (or the rapid-
impact package) for NTD control, especially
given the benefit of deworming in terms of
improving birth outcome and reducing
maternal morbidity and mortality [36,37].
The anthelminthic drugs mebendazole and
albendazole can be used in the second and
third trimester of pregnancy and are recom-
manded by WHO in the appropriate settings
[40]. Community-based prevention efforts
could also be integrated. Both untreated
bed-nets and LLITNs are proportionately
more effective in preventing lymphatic
filariasis compared with malaria [41], and
the use of bed-nets was shown to increase
substantially, in some cases 9-fold, when
used alongside NTD control efforts [42].

Together, malaria and the seven most
common NTDs listed above cause almost
2 million deaths and are responsible for the
loss of almost 100 million disability-adjust-
life years (DALYs) annually (almost 20% higher than the disease burden from HIV/
AIDS) [23]. Much of this high disease
burden operates through the mechanism
of anemia. According to J. Crawley, "...an
integrated and non-disease specific ap-
proach is essential if the intolerable burden
of anemia that currently exists in malaria-
endemic regions of Africa is going to be
reduced" [43]. Although there will be
operational challenges to integrating NTD
with malaria control, the opportunities for
improving health, education, and economic
development for the poorest people in sub-
Saharan Africa are simply too great for us
to ignore. Accordingly, the public–private
partnerships of the Global Network for
NTDs are working to identify opportunities
for integration [18]. In addition, given the
ability of hookworm and other NTDs to
interfere with vaccine immunogenicity, we
also need to consider the importance of
NTD research for the malaria research
agenda [44], as well as the opportunity to
develop new NTD drugs and vaccines
alongside new innovations in malaria
treatment and prevention [45].

It is likely that focusing control efforts
on malaria alone will thwart global efforts
to sustain malaria control, much less
achieve eradication. Ultimately, by reduc-
ing anemia in sub-Saharan Africa, linking
the NTDs with malaria control would have
a major impact on almost all of the
Millennium Development Goals [20]. It is
some four years since this approach was
suggested [19], but policy makers are only
gradually recognizing the benefits of more
holistic approaches to tackling the diseases
of the poor. An integrated control pro-
togram for tropical anemia in Africa repre-
sents one of our better hopes for a quick
win in the fight for sustainable disease
control and poverty reduction.

References


