# Correspondence

## Rapid Diagnostic Tests for a Coordinated Approach to Fever Syndromes in Low-Resource Settings

To THE EDITOR—We read with interest the editorial commentary by Crump [1], which emphasizes the need for a syndromic approach to fever in low-resource settings—citing 2 recent epidemics of *Salmonella* Typhi [2, 3], the decreasing proportion of malaria-attributable illness in many areas, and changing vaccination patterns as arguments. We strongly agree with this point and wish to emphasize the role of microbiologic diagnostic tests in this process.

Although the benefits of parasitological diagnosis of malaria are widely emphasized [4], using malaria diagnosis alone as the cornerstone of linking febrile patients to appropriate care is dangerous. For example, the Institute of Tropical Medicine, Antwerp, was recently asked for assistance by colleagues in the remote Bwamanda health zone of the Democratic Republic of the Congo, which was facing an outbreak of severe malarial anemia in the second half of 2011. A dramatic increase in blood transfusion requirements and in-hospital mortality was observed among children <5 years of age with parasitologically confirmed malaria. Intensified surveillance of bloodstream infections in December 2011 via the national reference laboratory in Kinshasa recovered 57 nontyphoidal *Salmonella* isolates among 135 blood cultures in severely ill children (42%). This large unrecognized outbreak of severe disease from a clonal strain of *Salmonella* illustrates the pitfalls of focusing on a single pathogen, such as malaria, in patients presenting with febrile illnesses in low-resource settings.

Further, widespread adoption of malaria rapid diagnostic tests (RDT) has resulted in dramatic increases in empiric antibacterial use among the three-quarters of febrile patients in whom no malaria is found [5]. This dichotomous diagnostic approach can only fuel emerging antimicrobial resistance in the settings that can least afford it [6].

Choosing rational empiric therapy for patients with febrile syndromes in low-resource settings is complicated by the fact that a large proportion of them may be caused by any of several geographically restricted infections and neglected tropical diseases, such as tick-borne borreliosis [7], visceral leishmaniasis [8], and human African trypanosomiasis. Such infections are severe and treatable but often clinically indistinguishable without confirmatory tests. Making matters worse, very little epidemiologic data underpin clinicians' assessment of prior probability in vast areas of Africa and Asia.

A syndromic approach to patients with fever that integrates relevant combinations of RDT is urgently needed in many parts of the world. This will require (1) comprehensive epidemiologic studies using reference standard techniques to determine the prevalence of priority diseases that are severe and treatable; (2) validation of existing RDT in field settings and development of new RDT for key pathogens of epidemiologic importance; and (3) evidence-based algorithms incorporating local epidemiological data and setting-specific RDT diagnostic contributions, because the latter can vary substantially by locality [9, 10].

We are working as part of the EU-funded NIDIAG (*N*eglected *I*nfectious *D*isease d*IAG*nosis) consortium to develop such an approach to persistent fever in 4 low-resource countries, with the aim of achieving patient-centered care pathways that will accelerate diagnosis and improve outcomes.

### Notes

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### References

1. Crump JA. Typhoid fever and the challenge of nonmalaria febrile illness in sub-Saharan Africa. Clin Infect Dis **2012**; 54:1107–9.
2. Neil KP, Sodha SV, Lukwago L, et al. A large outbreak of typhoid fever associated with a high rate of intestinal perforation in Kasese district, Uganda, 2008–2009. Clin Infect Dis **2012**; 54:1091–9.
3. Lutterloh E, Likaka A, Sejvar J, et al. Multidrug-resistant typhoid fever with neurologic findings on the Malawi-Mozambique border. Clin Infect Dis **2012**; 54:1100–6.
4. WHO. Guidelines for the treatment of malaria. 2nd ed. Geneva, Switzerland: World Health Organization **2010**:1–194.
5. D'Acremont V, Kahama-Maro J, Swai N, Mtasiwa D, Genton B, Lengeler C. Reduction of anti-malarial consumption after rapid diagnostic tests implementation in Dar es Salaam: a before-after and cluster randomized controlled study. Malar J **2011**; 10:107.

6. Vlieghe E, Phoba MF, Tamfun JJ, Jacobs J. Antibiotic resistance among bacterial pathogens in Central Africa: a review of the published literature between 1955 and 2008. Int J Antimicrob Agents **2009**; 34:295–303.
7. Vial L, Diatta G, Tall A, et al. Incidence of tick-borne relapsing fever in West Africa: longitudinal study. Lancet **2006**; 368:37–43.
8. Marlet MV, Sang DK, Ritmeijer K, Muga RO, Onsongo J, Davidson RN. Emergence or re-emergence of visceral leishmaniasis in areas of Somalia, northeastern Kenya, and southeastern Ethiopia in 2000–01. Trans R Soc Trop Med Hyg **2003**; 97:515–8.
9. Gamboa D, Ho MF, Bendezu J, et al. A large proportion of *P. falciparum* isolates in the Amazon region of Peru lack pfhrp2 and pfhrp3: implications for malaria rapid diagnostic tests. PLoS One **2010**; 5:e8091.
10. Chappuis F, Rijal S, Soto A, Menten J, Boelaert M. A meta-analysis of the diagnostic performance of the direct agglutination test and rK39 dipstick for visceral leishmaniasis. BMJ **2006**; 333:723.

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