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CORRESPONDENCE

Causes of Fever in Outpatient Tanzanian Children

TO THE EDITOR: As physicians working in the only public emergency department in Tanzania, we are acutely aware of the need for better data to guide management of febrile illness in children, as described by D'Acremont et al. (Feb. 27 issue).[1] However, we question the suggestion that it is safe to send febrile children home without antimicrobial treatment. In this study, 22% of febrile children had bacterial infections, and 10.5% had malaria. Since Tanzania has limited pediatric health care capabilities, follow-up cannot be ensured, and delayed treatment can lead to severe morbidity and mortality. In addition, in the studies that the authors cite to support the withholding of antimalarial drugs, investigators used rapid diagnostic testing,[2-4] which is often unavailable. In the studies that they cite to support the withholding of antibiotics, the children had respiratory symptoms,[4,5] not nonspecific febrile illness. Furthermore, since most medications are available without prescription, children often receive antimicrobial drugs before they arrive at a health center; the exclusion of children with previous treatment further limits generalizability. At this time, we would hesitate to support changing clinical practice.

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No potential conflict of interest relevant to this letter was reported.

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THIS WEEK'S LETTERS

TO THE EDITOR: D'Acremont et al. used extensive investigations to reveal the diverse microbiologic ecology of febrile illness among Tanzanian children. In the same issue of the *Journal*, Maitland's editorial takes a developing-world perspective.[1] We believe both viewpoints are equally relevant to well-resourced settings in which the use of readily available new diagnostics is often guided by scarce clinical evidence. In a U.S. setting, viral polymerase-chain-reaction (PCR) assay identified at least one virus in 76% of febrile children but also notably in 35% of afebrile children. In-

terestingly, 51% of the children with a virus and no apparent bacterial infection received antibiotics.[2] Gene-expression profiling also remains unproven in an undifferentiated clinical context.[3] Conversely, the high negative predictive value of nasal PCR for methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia shows how new diagnostics might direct clinical management.[4]

D'Acremont et al. call for more point-of-care tests. Since they identified a possible cause in 97% of febrile children, we agree with Maitland that the greater need is for case–control studies, differentiating pathogens from passengers, and research assessing the value of new diagnostics in clinical decision making.

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No potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: It is our opinion that D'Acremont et al. may have underestimated the prevalence of bacteria causing upper or lower respiratory tract infections for several reasons. First, naso-oropharyngeal specimens were tested for 14 respiratory viruses but for only one bacterium, *Streptococcus pneumoniae*. The investigators did not test for additional bacterial causes of respiratory infection, such as *Haemophilus influenzae*, *Staphylococcus aureus*, *Bordetella pertussis*, and *Mycoplasma pneumoniae*. Second, although chest radiography confirmed the diagnosis of pneumonia, sputum specimens were not collected and tested for bacterial identification. Third, blood culture was performed only in patients in whom respiratory illness had been excluded. The collection of additional respiratory specimens,[1] testing for more than one bacterium with the use of more sensitive molecular methods,[2-4] and an extended study duration would provide a better understanding of the contribution of bacteria among these children. We agree that it is important to avoid unnecessary treatment of viral infections with antimicrobials, but it is also important not to miss the opportunity to provide lifesaving antibiotics.

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THE AUTHORS REPLY: We agree with the correspondents that children who need antibiotic treatment should receive it as soon as possible. However, we would like to clarify that the goal of our study was not to test a clinical strategy for antibiotic prescription but rather to provide a thoughtful description of the origin of fever in a population that is likely to be prescribed antibiotics.

Our study included a spectrum of inpatients and outpatients. Since the latter represent the vast majority of patients, we attempted to reflect the overall burden of disease encountered by the health system and not the smaller proportion of hospitalized children with severe disease who are often the target population of clinical studies. In our study, children with mild illness indeed had a much lower rate of bacterial disease (16%) than did children with severe illness (60%). To establish causality between pathogens (viruses, bacteria, or parasites) that were identified and a given febrile episode is challenging, especially in young children with acute respiratory infections in whom

bacterial colonization on PCR assay is frequent (88% positive for pneumococcus) and sensitivity of blood culture is low. A control group would have helped to identify the background level of carriage but would not have solved the problem of causality at the individual level.

Although our study was not designed to respond to the question of who would benefit from antibiotics, we know that 363 of the 576 children with evidence of viral disease did not receive antibiotics and that only 4 of them were still febrile at day 7. To our knowledge, no study has yet assessed whether antibiotics can be withheld in children with nonsevere febrile illness, but the findings from studies in Europe, where children rarely receive antibiotics in an outpatient setting,[1] and from studies at the community level in Africa[2] are reassuring. Our study suggests that we need to better identify the subgroup of children who will benefit from empirical antibiotic use among the numerous children with self-limited disease.[3]

We provide evidence for potential revision of clinical decision charts, ideally supplemented by new diagnostic tools. Also, because severe morbidity in young children with acute respiratory infection is mostly due to bronchiolitis or viral pneumonia, as suggested by our study and others,[4] the availability of oxygen would probably save more lives than the systematic provision of antibiotics.[5] A more rational use of antimicrobials is urgently needed if we want to slow down the dramatic progression of antibiotic resistance in Africa and worldwide.

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Since publication of their article, the authors report no further potential conflict of interest.

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Management of Skin Abscesses

TO THE EDITOR: The review by Singer and Talan (March 13 issue)[1] describes the management of skin abscesses in the era of methicillin-resistant *Staphylococcus aureus* (MRSA).[1] In a 3-year study of soft-tissue and invasive infections caused by Panton–Valentine leukocidin (PVL)–positive methicillin-susceptible *S. aureus* (PVL-MSSA) and MRSA in a pediatric hospital, we found that PVL is largely diffused in both community-associated MRSA (CA-MRSA) and in MSSA,[2,3] as has been described,[4] and MRSA genotypes have a particular distribution in different geographic regions.[5] In our experience, PVL-MSSA strains were more frequent than PVL-MRSA, with all the latter belonging to already described clones such as USA300, Pediatric, and South West Pacific. Collected strains showed a low level of in vitro resistance against common antimicrobial agents, as is usually found in CA-MRSA. The outcomes of both PVL-MRSA and PVL-MSSA soft-tissue and invasive infections were similar, either when surgery was required or when antimicrobial agents that inhibit the production of toxins were administered (Table 1). Therefore, we believe that cultures of any drainage should be obtained, when possible, and PVL testing should be performed.

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