MINI-REVIEW

Public health impact of establishing the cause of bacterial infections in rural Asia

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Summary Recent studies delineating bacterial causes of fever in rural Asia indicate a major role for several previously under-recognized pathogens, including \textit{Rickettsia} and \textit{Leptospira}. The use of blood culture for the first time to investigate patients with febrile illness in rural Asia has also revealed some unexpected findings, e.g. \textit{Staphylococcus aureus} is the major cause of bacteraemia in children aged <1 year in Laos. The spread of antimicrobial-resistant pathogens such as MRSA into rural Asia has already occurred and requires monitoring. These factors have major implications for empirical therapy of fever. Initiatives are urgently needed to strengthen the infrastructure of microbiology in rural Asia.

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The development of diagnostic microbiology laboratories is low on the list of health-care priorities across rural Southeast Asia. By contrast, there has been considerable progress in determining the optimum diagnostic techniques and therapy for malaria in the region. This has led to the situation where the main uncertainty facing malaria-orientated primary health care workers in rural Asia is how to treat patients when the fever is not due to malaria. Treatment of acute febrile illness in patients with a negative malaria blood film/rapid diagnostic test is usually empirical. The importance of studies that define causes of bacterial infection in this setting has gone unrecognized and is unattractive to most funding agencies, but the publication of several recent studies indicates a need to review attitudes towards laboratory diagnosis in rural Asia.

Studies conducted in Laos, Nepal and Thailand provide strong evidence that rickettsial infections such as murine and scrub typhus, previously under-recognized and under-reported, are major causes of febrile illness. Acute rickettsial infection was identified as the cause of fever in 115/427 (27%) adults with negative blood cultures admitted to Mahosot Hospital in Vientiane, Laos (Phongmany et al., 2006). These findings were echoed in five provincial hospitals in Thailand (Suttinont et al., 2006). Two studies in Nepal also reported the incidence of rickettsial infections in patients presenting with febrile illness. In a study of 103 patients, scrub and murine typhus were diagnosed in 22 and 26% of cases, respectively (Blacksell et al., 2007). In a second study of 879 febrile patients, scrub and murine typhus were diagnosed in 3 and 11% of cases, respectively (Murdoch et al., 2004).

Leptospirosis has emerged as a major cause of febrile illness in rural Asia and was reported as the cause of fever in...
37% of 845 patients presenting to hospitals in provincial Thailand (Suttinont et al., 2006). Leptospirosis has been reported in Nepal as the cause of fever in 10/103 patients and 36/879 patients in two studies (Blacksell et al., 2007; Murdoch et al., 2004). These findings have considerable practical importance, as these pathogens are likely to respond to relatively inexpensive courses of tetracyclines.

More information on bacterial disease patterns in rural Asia is the result of studies in which blood cultures are used for the first time to investigate patients with febrile illness. Some findings are predictable; for example, *Salmonella enterica* serotype Typhi predominates as the cause of bacteraemia in Nepal and Laos (Murdoch et al., 2004; Phetsouvanh et al., 2006). However, some findings are unexpected, e.g. that *Staphylococcus aureus* was the most common cause of bacteraemia in infants under the age of 1 year (69.2%) in a study in Laos (Phetsouvanh et al., 2006). *Staphylococcus aureus* is also a major cause of bacteraemia in provincial Thailand, where more than 20% of cases are caused by methicillin-resistant *S. aureus* (MRSA). MRSA has now appeared in both Laos and Cambodia. Melioidosis, a life-threatening infection caused by the Gram-negative bacillus *Burkholderia pseudomallei*, is well described in northeast Thailand but has recently become recognized in Laos and Cambodia as a direct result of the introduction of blood culture facilities.

These landmark studies indicate a major role for several previously under-recognized pathogens, revealed by ‘emerging’ microbiologists. Many infections in a tropical setting are clinically indistinguishable; defining the true pattern of infectious diseases is essential to the development of effective policies for the empirical treatment of fever. The spread of antimicrobial resistance into resource-poor areas, where the antibiotics used often have a limited spectrum of activity, is fuelled by widespread availability of over-the-counter antibiotics in rural Asia. Documenting the scale of resistance is a central function of the microbiology laboratory. There is a lack of information on the burden of disease caused by bacterial pathogens and resistance patterns in many countries in this region, including Sri Lanka, Bangladesh, Burma (Myanmar), Cambodia and Indonesia. The development of microbiology laboratories attached to hospitals and tailoring individual patient care to microbiological testing is unrealistic, but a network of laboratories dedicated to the delineation of infectious disease epidemiology in different Asian environments is not. This initiative would entail reconsideration of diagnostic technology. Recognition of rickettsial infections and leptospirosis currently depends, problematically, on detection of antibody responses in acute and convalescent sera. More accurate, inexpensive, rapid and simple tests for common and treatable infectious diseases are urgently required to allow health workers to diagnose and treat appropriately the multitude of clinically similar diseases in Asia; in recent studies the cause of fever was unknown in 50% of patients. As effective artemisinin-based combination therapy is introduced into the vast diversity of sub-Saharan Africa, similar questions will need to be addressed there on the causes and therapy of non-malarial fever.

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References


