because the expertise and facilities for clinical and laboratory diagnosis of Hib infections are inadequate. However, innovative methods have been developed to define Hib disease burden, and these have proven useful for making informed decisions about vaccine introduction and impact evaluation in these countries.

## Hospital and Community-Based Surveillance for Hib Disease

Hospital-based surveillance for bacterial meningitis defines the proportion of children admitted with Hib meningitis at a particular hospital for a given period of time. This must be based on documented definitions, clinical and laboratory investigations including a record of history and, when possible, a biological test for prior antibiotic use. Incidence of Hib meningitis cannot normally be calculated because the patient catchment population is usually difficult to define. When the hospital facility is contained within a well-defined catchment population, the incidence of Hib disease, particularly of meningitis, can be estimated after adjustment for access to care. The comparability of surveillance data in different areas is dependent on consistency in patient selection and enrolment, and laboratory investigations to ensure that eligible patients are captured and investigated appropriately. A generic protocol was developed by WHO in 1996 for in-country assessment of disease burden for Hib meningitis (30). The protocol contains guidelines for selection of surveillance sites and information on clinical, laboratory, and epidemiological methods, and has been made accessible electronically (31). The main limitation of this method is that Hib disease due to pneumonia cannot be adequately measured, and in many developing countries a significant proportion of meningitis cases die at home without accessing care.

Because the syndromes of clinical meningitis and pneumonia are not etiology specific, clinical findings alone are not sufficient to diagnose Hib disease. Therefore, clinical suspicion of meningitis or pneumonia must be accompanied by collection of appropriate specimens such as CSF and blood, respectively, for laboratory isolation of the bacterium or detection of bacterial antigens using latex agglutination tests. Polymerase chain reaction (PCR) methods can be used when available for direct detection of Hib in CSF. In contrast, the confirmatory diagnosis of Hib pneumonia is more problematic. Available clinical and radiological methods lack sensitivity or specificity. Although laboratory isolation of Hib from blood of patients with clinical evidence of pneumonia can be definitive, the sensitivity is poor and the level of expertise required is often lacking in many developing countries (32,33). For these reasons, surveillance for Hib disease is often targeted at meningitis alone.

## Population-Based Surveillance

Despite its limitations, blood culture surveillance for invasive bacterial disease has shown that Hib is a major cause of bacteremia in children in Africa. Population-based studies have been used to document Hib disease burden as a major cause of morbidity and mortality in several countries including Kenya, Mali, and The Gambia. At a district hospital located in an area with a well-defined catchment population on the coast of Kenya, acute bacterial infections were a common cause of admission to the hospital. Blood was cultured from 19,339 patients on admission to hospital between 1998 and 2002. Hib accounted for 12% (136 of 1132) of bacterial isolates from among children aged less than five years, and for 19% (18 of 103) of isolates from among children who died in hospital on the day of admission (34). The annual incidence of Hib bacteremia was 159, 120, and 60 per 100,000 children aged less than one year, two years, and five years, respectively. The incidence of acute bacterial infections caused by Hib was eclipsed only by those of pneumococcus and nontyphoidal *Salmonella* in children less than five years. In children aged two months to one year, Hib was of the same rank with pneumococcus among bacterial species isolated from patients with bacteremia (34).

Similarly, in Mali, the age-specific incidence of Hib disease was determined after the establishment of a bacteriology laboratory in the main hospital serving Bamako, the capital city. The study investigated 3592 children admitted to the hospital over a two-year period with suspected invasive bacterial disease. Hib was isolated from 207 children; 98% of these were aged less than five years, and 60% (124) were meningitis cases. The annual incidence of Hib disease per 100,000 child years was 45 among children less than five years, and 158 among children aged less than one year. The peak incidence, 370/100,000 person years, was found among children aged six to seven months, and 12 (57%) of 21 recorded Hib deaths also occurred in this age group (35).

As noted earlier, the incidence of Hib meningitis was high in The Gambia prior to vaccination, with a rate of 297/100,000 per year among children aged less than one year and 60/100,000 among children less than five years (12). The disease occurred mainly in younger children; 84% of cases were aged less than 12 months and 45% were less than six months. Neurological sequelae were common. The case fatality rate was 30%, and only 45% recovered completely from Hib meningitis (36). Pneumonia was more common and its outcome was worse in Gambian children than in the developed countries. In common with most of the other developing countries, epiglottitis was rarely seen (37).

## Other Approaches to Disease Burden Assessment

The Hib rapid assessment tool (Hib RAT) was developed by WHO to estimate the local burden of Hib disease and mortality where population-based estimates are not available (38). The tool uses two complementary methods to achieve these objectives. The first method uses routine hospital meningitis data within a well-defined population to estimate the local incidence of Hib meningitis, then inflates this figure by a factor of five to estimate Hib pneumonia incidence and extrapolates these rates across the country. The second method uses the under-five mortality rate, if known, to calculate the number of deaths caused by acute respiratory infections, and then estimates that 13% of these deaths are caused by Hib. A Hib RAT is usually completed in 7 to 10 days by a team of two to three local health officials and one to two consultants. The accuracy of the Hib RAT is dependent on the quality of local Hib disease data. In Africa and some countries of the Middle East, Hib RAT meningitis incidence rates have been similar to estimates from population-based studies in these regions. In contrast, variable Hib RAT estimates have been obtained from Eastern Europe and Asia, where Hib meningitis appears to be less well defined (38). Despite its limitations, the Hib RAT has been used by several countries in Africa to provide baseline data on Hib disease prior to vaccine introduction. The Hib RAT manual, including calculation worksheets, is available from WHO (39).

Sentinel site surveillance was established for Hib meningitis by the WHO pediatric bacterial meningitis surveillance