Japanese encephalitis (JE), a mosquito-borne viral brain infection, afflicts an estimated 35,000 to 50,000 inhabitants of Asia and the western Pacific annually. The disease most often strikes children, who have not yet built up a natural immunity. One-third of JE infections are fatal, and another third leave survivors with severe neurological sequelae. There is no treatment for JE; vaccination is the only defense. Funded by the Bill & Melinda Gates Foundation, PATH’s JE project (2003–2009) worked with international partners and developing countries to increase the information available for understanding the extent of the disease and how best to control it.

JAPANESE ENCEPHALITIS DISEASE SURVEILLANCE

Background

JE disease can have significant consequences, with a mortality rate of as much as 30% or higher and life-changing physical and cognitive disabilities borne by as many as half of JE survivors. Assessment of disease burden is important for governments’ decision-making about vaccine introduction, but JE surveillance is complicated by a number of factors. There are no JE-specific clinical presentations; rather, it is one of several etiologies of acute encephalitis syndrome (AES). A JE diagnosis can only be confirmed through laboratory testing of cerebrospinal fluid (CSF) or of serum samples, the latter taken during both the acute and recovery phases of illness. This presents a challenge to countries with limited capacity.

Even before specimens reach a lab, endemic countries face logistical challenges of transportation while maintaining the cold chain. Compounding these difficulties is the cross-reactivity of the dengue virus (also a flavivirus), which often co-circulates in JE-endemic areas. Additionally, a lack of reporting standards can prevent collection of standardized data. Overcoming these challenges has been an important part of PATH’s JE project.

Setting standards for syndromic surveillance

With the variability among clinical presentations of JE infection, a standard clinical case definition for AES is a vital first step in identifying possible cases. Laboratory testing then distinguishes JE from other neurological infections. These elements are outlined in the World Health Organization (WHO) JE surveillance standards.

Increasing diagnostic capacity

The refinement of JE diagnostic tests and capacity-building of regional laboratories were important efforts of the JE project. PATH assisted in the evaluation of sensitivity and specificity among diagnostic kits and the development of a validation panel to assist national-level use of in-house diagnostic kits.

Helping countries measure the extent of JE

PATH has worked to help national programs begin or enhance JE surveillance. Increased efforts in Cambodia, Indonesia, Nepal, and Vietnam provided insights into the burden of JE disease to inform decision-making on immunization.

Revealing nationwide disease burden: Indonesia

In Indonesia, the presence of JE throughout the country was in question, but a two-year surveillance study showed JE as an endemic disease nationwide. Sentinel surveillance conducted by PATH and the National Institute for Health Research and Development recorded JE cases in six provinces throughout the country, with risk varying according to geographic region. Further research evaluated the additional disease burden caused by post-JE disability—an often-overlooked aspect that leaves a significant impact on families and communities. Among JE survivors studied, 25% experienced sequelae so severe they were unlikely to lead independent lives.

Applying surveillance data toward program planning: Cambodia

With PATH and WHO assistance, Cambodia’s Communicable Disease Control Department and the National Institute of Public Health established sentinel surveillance at six sites in 2006. By 2007, the data showed clear evidence of disease burden, with children younger than 12 years of age at highest risk. At a meeting to disseminate the results, participants committed to developing a national JE control plan, with vaccine introduction in 2009. PATH collaborated with researchers in Cambodia to analyze and disseminate surveillance results through a series of publications. Surveillance became the responsibility of the National Immunization Program in 2009, and JE vaccine was introduced on a small scale in October 2009, with plans for future expansion.

Gathering data to evaluate program performance: Vietnam

Vietnam began AES surveillance in 1979 and conducted several studies in the mid-1990s, including one in northern Vietnam that showed more than half of AES cases were JE. The National Expanded Programme on Immunization introduced the mouse brain–derived JE vaccine in 1997 for 11 high-risk districts.
PATH provided technical assistance to strengthen the existing AES surveillance program, supporting the National Institute of Hygiene and Epidemiology in developing JE surveillance guidelines, identifying two initial sites, and conducting training. An additional sentinel site was added in 2008, creating a system that covers three provinces in the northern, central, and southern regions. Routine and standardized surveillance informed expansion of the immunization program, which now covers 267 districts in 50 provinces.

Enhancing existing surveillance systems
Funding from PATH’s JE project allowed many other countries to capitalize on WHO’s extensive surveillance experience. With financial support from PATH, WHO regional offices supported system enhancement through inclusion of surveillance for AES and/or JE in Bangladesh, Bhutan, Cambodia, China, India, Laos, Nepal, Papua New Guinea, Philippines, Timor L’este, and Vietnam.

These activities generated data crucial to JE control strategies. In Nepal, for example, integrated field- and laboratory-based AES surveillance within the existing vaccine-preventable diseases surveillance system resulted in greater collection of diagnostic specimens and more follow-up investigations after illness. The resulting clarity on disease burden prompted Nepal to hold JE vaccination campaigns in 2007 and 2008.

Looking to the future
PATH has also focused on developing an up-to-date global incidence estimate for JE. While universal estimates have been produced before, the most recent one is nearly 20 years old. For proper health planning, a more accurate and data they need to protect their populations from JE.

Lessons learned
- Clear surveillance standards provide critical guidance and ensure collection of accurate and useful disease burden data.
- Building surveillance and diagnostic capacity in endemic regions generates increased accuracy of disease burden data and sustainability of standardized data collection.
- Surveillance data help endemic countries learn about their own JE burden and plan targeted interventions, which can then be monitored for impact based on rates of disease incidence.
- The disease burden of JE involves not only the acute disease, but also its devastating aftereffects such as sequelae and long-term disability.

ENDNOTES