

# COMBATTING JAPANESE ENCEPHALITIS IN NEPAL:

a public health success story



## NEPAL'S COMMITMENT TO VACCINATION TURNS THE TIDE AGAINST A DREADED "BRAIN FEVER."

In 2005, a devastating Japanese encephalitis (JE) outbreak took the lives of nearly 2,000 people—mostly children—living in poor, rural districts of the Terai in southern Nepal and northern India. Just a few years later, however, the number of JE cases in Nepal began to plummet, and not a single JE death has been recorded in Nepal since 2010. The reason for this rapid progress? Expanded use of a safe, effective JE vaccine and the government's unwavering commitment to its use.

JE, a type of "brain fever," results from a virus transmitted to humans by mosquitoes. The mosquitoes, which breed in stagnant water common in rural areas with rice paddies, get the virus by biting infected pigs and water birds and then spread it to humans. The disease begins like the flu and progresses to affect the brain, killing up to 30 percent of its victims and leaving up to half of its survivors with permanent brain injury that can cause paralysis, seizures, inability to speak, and other serious neurologic disabilities. Providing lifelong care for survivors is a tremendous financial strain on families and Nepal's health care system.

Today, an estimated 12.5 million people in Nepal are at high risk for JE. The JE-endemic region has expanded from 24 districts in the Terai—the plains south of the Himalayan foothills—to districts in the bordering hills and mountains to the north, including the heavily populated Kathmandu Valley.<sup>1</sup>

The 2005 outbreak increased national and international attention to the disease. Over the next decade, Nepal made tremendous progress in JE prevention. Through surveillance, introduction and expansion of JE vaccination, and improved case management, the country has significantly reduced JE morbidity and mortality.

While Nepal shares many characteristics with other JE-endemic countries struggling to contain the disease—such as limited financial resources and health care infrastructure—the country's JE prevention and control program has been a shining success. Routine JE vaccination has already saved the lives of thousands of children in Nepal and prevented even more disabilities, and the government of Nepal continues to demonstrate its commitment to combatting JE by expanding its JE vaccination program to all 75 districts.

So, how did Nepal do it? This case study details Nepal's efforts against this disease—from establishing disease surveillance to a robust routine JE immunization program—despite several challenges.



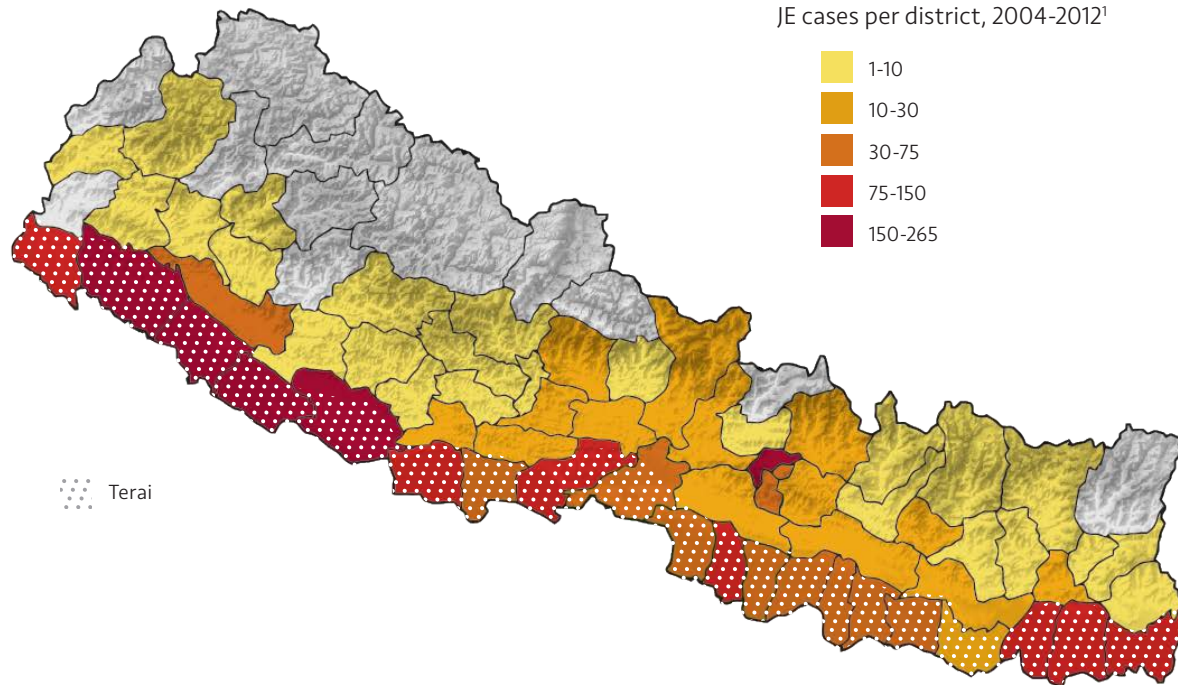
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### THE EARLY YEARS OF JE IN NEPAL

The first recorded JE epidemic in Nepal occurred in 1978 in Rupandehi District along Nepal's southwestern border with India.<sup>1</sup> Subsequent epidemics were noted in the eastern Terai and eventually in all 24 Terai districts. Because diagnostic laboratory tests for JE virus infection were not yet available in Nepal, the initial JE cases were merely "suspected" based on clinical symptoms of acute encephalitis syndrome (AES). Nepal implemented national AES surveillance using a standardized case definition (fever with deterioration in mental status and/or new onset of seizures<sup>2</sup>) following the 1978 epidemic. AES case reports were sent to the Nepal Ministry of Health (MOH) every quarter, and a picture of the disease burden began to emerge. These early efforts helped the government of Nepal understand that JE needed to be addressed.

**Figure 1. Burden of JE in Nepal**

JE cases per district, 2004-2012<sup>1</sup>



### **PATH's role in Nepal's JE program**

Funded by the Bill & Melinda Gates Foundation, PATH's work to combat JE provided technical assistance to Nepal, from strategy development through program implementation and evaluation. In addition, PATH helped negotiate the low, public-sector price for CD-JEV, which allowed Nepal to purchase the vaccine for its JE immunization program.

A unique opportunity for Nepal arose in 1999. China's Chengdu Institute of Biological Products (CDIBP) had developed a live attenuated JE vaccine (CD-JEV) that was more effective and less expensive than previous JE vaccines. Following CD-JEV's 1988 introduction in China, JE mortality and morbidity in China declined rapidly. In 1999, because of the high burden of JE in Nepal, CDIBP donated 224,000 doses of CD-JEV vaccine to the government of Nepal. Using donated vaccines, government health clinics conducted vaccination campaigns in July of that year for children 1 to 15 years old in three western Terai districts.<sup>1,2</sup> Recognizing the potential of this vaccine, the MOH conducted a vaccine effectiveness study. Funded by Glaxo Biotech Corporation, the study found that CD-JEV was 99.3 percent effective in preventing JE following just one dose.<sup>3</sup>

Based on this vaccine effectiveness study and the impact of the JE vaccination campaign, Nepal knew that vaccination was the best way to prevent JE. However, the country also knew that it needed a long-term, sustainable vaccination

program directed by the JE-specific disease burden rather than AES burden. To identify districts with the highest JE incidence that are in greater need of vaccination campaigns, the national surveillance program needed to add laboratory testing to identify JE virus as the specific cause of AES. Utilizing technical assistance from Nepal's World Health Organization (WHO) country office and existing laboratory infrastructure and personnel from the polio and measles surveillance program, JE laboratory testing was introduced to 64 referral hospitals throughout the country in 2004.<sup>2</sup> By sending samples to national laboratories, clinical encephalitis cases due specifically to JE virus could be identified for the first time, providing policymakers with much-needed data on the epidemiology of JE in the country (Figure 1).

*"The surveillance program was a success because people knew JE was a problem, and they were terrified of it. They were eager to implement the surveillance because they wanted to know what the burden was and what they could do about it."*

-Thomas Wierzbza, head of WHO-IPD in Nepal from 2003-2006

### **THE PUSH FOR ROUTINE JE IMMUNIZATION**

In 2005, a severe JE outbreak on the border between Nepal and India claimed thousands of children's lives and roused international media attention on JE. Following the outbreak,

## Overcoming perceived barriers through creativity

High-level decision-makers in JE-endemic countries often cite four main barriers for JE vaccine introduction. Nepal overcame all of them.

### 1. Lack of surveillance data to determine disease burden and diagnostic laboratory testing capabilities to confirm JE cases.



While Nepal lacked surveillance data and laboratory testing capacity at the outset, the country prioritized JE surveillance and set up a robust JE surveillance system by utilizing existing disease surveillance networks and partnering with WHO. Improved surveillance uncovered an unexpected burden of JE among adults in addition to children.

### 2. Inadequate financial resources and health infrastructure capacity to introduce vaccination.



Despite limited finances, Nepal introduced JE vaccine because decision-makers knew it would be highly cost-effective compared to the cost of managing JE cases and accommodating lifelong neurologic disabilities. Nepal was able to save even more by introducing CD-JEV, which has a low public-sector cost and one-dose regimen, and by utilizing its existing infrastructure and human resources from polio eradication efforts. Once it became available, Nepal utilized Gavi financing to expand JE vaccination to additional districts.

### 3. Competing policy priorities around introducing other vaccines.



Decision-makers in Nepal prioritized JE vaccines because of the significant burden in the country, but they knew that introducing multiple vaccines was feasible through coordination. Through careful planning and evidence-based decision-making, Nepal coordinated JE vaccine introduction alongside other lifesaving vaccines. In doing so, Nepal was able to maximize protection of its children.

### 4. Need for technical assistance and training materials to guide JE vaccine introduction.



When Nepal needed technical assistance with designing its JE vaccination program, the government sought the assistance and expertise of WHO. With this help, the MOH designed an evidence-based phased vaccination scale-up plan and developed materials to train health workers along the way.

the Nepal MOH knew it needed to expand and accelerate its JE control plans. Using data from the laboratory-based surveillance, Nepal devised a plan to add CD-JEV to its Expanded Program on Immunization (EPI) for children in high-risk districts.

One year after the devastating 2005 epidemic, the government of Nepal purchased CD-JEV directly from CDIBP and officially launched Nepal's JE vaccination program in a few high-burden endemic districts. Since the vaccine had not yet been prequalified by the WHO, JE vaccine support from Gavi, the Vaccine Alliance was not yet available. Instead, Nepal applied for a loan from the World Bank and purchased the vaccine at an affordable public-sector price that had been previously negotiated by PATH for low- and lower-middle-income countries.

Under the MOH's plan, initial campaigns were focused on areas with high JE incidence and large populations. In addition to health worker trainings, public outreach and education, and supply chain improvements—all of which were critical to successful vaccine introduction—Nepal also strengthened its surveillance systems to collect strong data to support its decisions throughout the campaigns. Based on these data and on the cold chain capacity and health worker availability within each district, JE vaccination campaigns were expanded in a phased manner (Figure 2).



PATH/Huong Vu Minh

Following the initial campaigns, CD-JEV was introduced into the EPI in 22 districts in 2009, and by 2012, routine JE immunization was established in 31 districts.<sup>1</sup> In 20 of those districts, the MOH made the decision to vaccinate all persons above one year of age, including adults. This decision was based



on surveillance data showing that, in some districts, there was a significant JE burden among adults in addition to children—something that medical authorities had not previously realized.

#### AN IMMEDIATE AND GROWING IMPACT

In the early campaigns in 1999, JE vaccination in Nepal showed powerful protection following just one dose. Confirming the findings of the first effectiveness study conducted during the campaigns, another study found that children were 99 percent less likely to contract JE one year after being vaccinated.<sup>4</sup> Even five years after vaccination, the children were still 96 percent less likely to become infected.<sup>5</sup>

After JE vaccination campaigns were introduced as part of the national immunization program in 2006, the number of JE cases in Nepal dropped significantly (Figure 3). An analysis of surveillance data from 2004 to 2009 found that, after the campaigns, JE incidence was 72 percent lower than would have been expected if campaigns had not occurred.<sup>6</sup> Additionally, AES incidence was 58 percent lower after campaigns, suggesting that a large proportion of encephalitis cases without laboratory confirmation may be caused by JE and that the impact of JE vaccination may be larger than previously thought.

The government's decision to target the entire population above one year of age in districts showing disease burden in older age groups also shows promising impacts. Compared to districts that only vaccinated children 1 to 15 years of age, JE incidence was significantly lower in districts vaccinating the entire population over 1 year of age.<sup>6</sup> While children suffer the greatest JE burden and should be prioritized for vaccination before adults, the JE burden in adults is being increasingly recognized, and Nepal's success suggests that

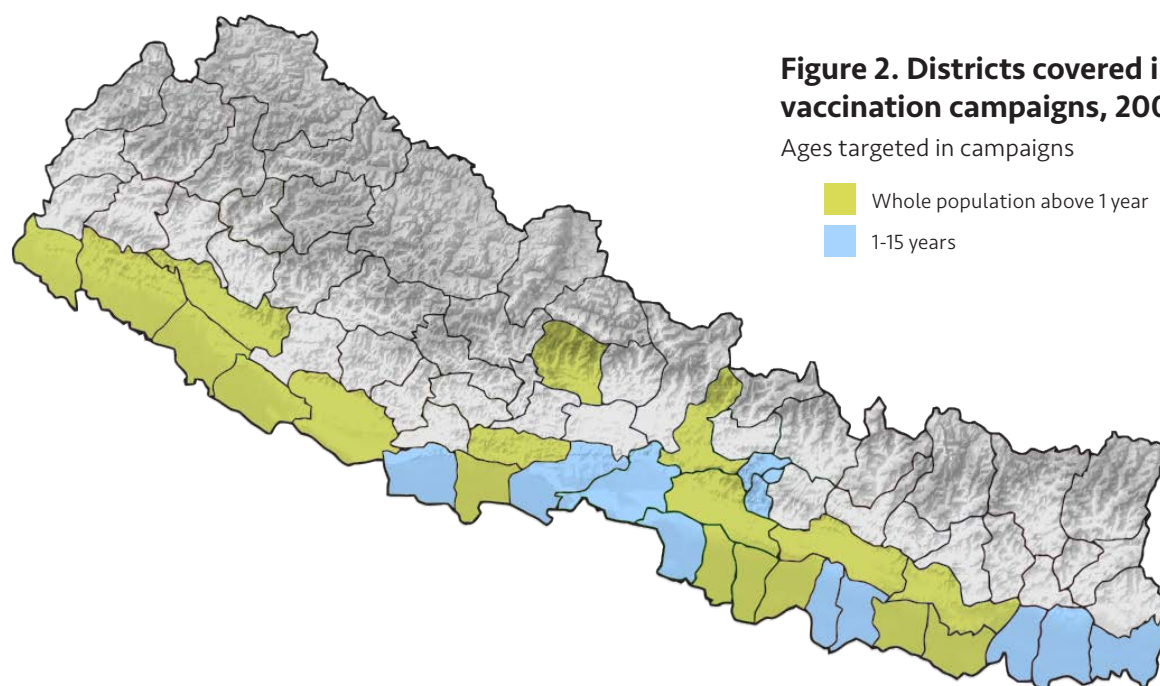
#### Projected impact by the numbers

Data from Nepal suggest that, for every 100,000 children given JE vaccine in the initial 23 districts over the next 30 years:<sup>6-8</sup>

- 107** laboratory-confirmed JE cases will be averted;
- 205** unconfirmed encephalitis cases due to JE will be averted;
- 79** fewer children will die from JE;
- 90** fewer people will have an abnormal neurology exam upon leaving the hospital after JE;
- 3,432** fewer days will be spent in a hospital due to JE; and
- \$261k** in out-of-pocket costs for treatment (US\$) will be saved by families.

vaccinating adults may be an effective strategy where a large proportion of cases in adults has been identified. "Surveillance data should always be processed to identify new at-risk groups. The decision to vaccinate adults as well as children in some districts has helped magnify the success of Nepal's JE immunization program," notes Dr. Jagat Narain Giri, immunization coordinator at WHO-IPD.

The impact of Nepal's JE vaccination program will only continue to grow. Nepal's EPI manager, Mr. Mukunda Raj Gautam, notes, "Vaccinating children against JE is a great investment in their future. In Nepal, we hope to one day see JE become a thing of the past."



**Figure 2. Districts covered in JE vaccination campaigns, 2006-2011<sup>1</sup>**

Ages targeted in campaigns

- Whole population above 1 year
- 1-15 years

## Keys to a successful scale-up

Dr. Rajendra Pant, chief of the Child Health Division at the Department of Health Services within Nepal's MOH, states, "The keys to success in combatting JE are greater community participation, government commitment, and the hard work of health professionals and community volunteers." Specifically, the following activities were vital to Nepal's success in scaling up a national JE vaccination program:



### Using surveillance data to guide implementation

By strengthening its JE surveillance systems to collect better JE-specific data, Nepal was able to support its decisions to conduct campaigns in districts at highest risk. Based on these surveillance data, JE vaccination campaigns were continuously adjusted and expanded.



### Integrating with existing surveillance and vaccine delivery systems

The Nepal MOH decided to use existing country resources originally designed for polio vaccination—including health workers, facilities, cold chain equipment, and logistics systems—toward control of JE.



### Training health workers and volunteers

Prior to each district's JE vaccination campaign, local health authorities, health workers, and volunteers were trained at district-level meetings. In addition to providing an overview of JE disease and vaccine handling requirements, the MOH armed health workers with social mobilization tools and expanded their roles in routine and supplementary immunization.



### Introducing a safety surveillance program

The MOH established surveillance for any adverse events following immunization at sentinel sites and all major hospitals. The government used these data to continually monitor the vaccine's safety.



### Implementing a JE awareness program

Nepal implemented a JE awareness program to encourage vaccination as part of its JE strategy. The MOH developed a variety of materials, including posters and vaccination invitation letters, for JE awareness in a variety of local languages. Local media outlets and interpersonal communications with health workers also helped spread the word about JE vaccines.



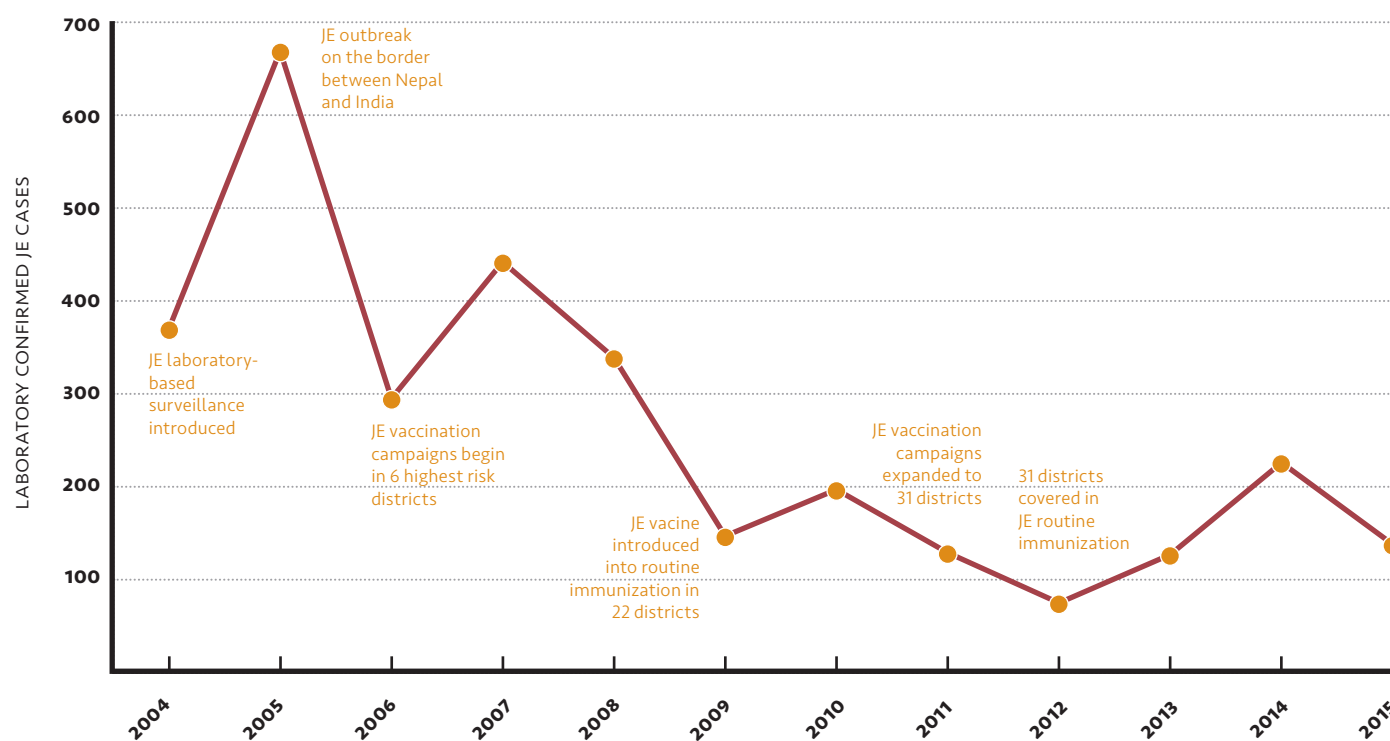
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## A BRIGHT FUTURE

Through surveillance and immunization, Nepal has made remarkable progress against JE in the past few decades. However, JE continues to spread to additional districts in Nepal—including those in the hills and mountains, which may prove more difficult to reach. The Nepal MOH is continuing to improve its JE prevention and control program in the following ways:

- **Expanding JE vaccination to additional districts.** In 2015, Nepal applied for funding from Gavi to expand its JE vaccination program to 47 of the 75 districts in Nepal. These campaigns began in May 2016 with the aim of vaccinating an additional four million children in 44 districts in Nepal and intensifying coverage in three Terai districts with existing routine JE immunization. Eventually, the country plans to expand JE into the routine immunization program nationwide.
- **Balancing JE vaccines with other new vaccines.** In addition to adding JE vaccine to its EPI schedule in 2006, Nepal also added pentavalent vaccine in 2009, inactivated polio vaccine in 2014, and pneumococcal conjugate vaccine in 2015. Through careful planning and evidence-based decision making, Nepal continues to coordinate JE vaccination alongside an ever-expanding list of other lifesaving vaccines and maximize protection of its children.
- **Ensuring continued safety of JE vaccines.** The WHO position paper on JE vaccines states that CD-JEV has an acceptable safety profile,<sup>9</sup> and studies evaluating CD-JEV in Nepal found the vaccine to be safe.<sup>2,3,4</sup> To ensure continued safety, Nepal's EPI has plans to intensify and strengthen safety surveillance in all districts with JE vaccination through the central and district immunization safety committees.<sup>1</sup>

**Figure 3: Impact of Nepal's JE vaccination program, 2004-2015\***



\*In May 2016, the government of Nepal began new JE vaccination campaigns in the remaining 44 districts of Nepal.

- Improving JE awareness through education.**  
 Education about JE and the availability of vaccines helps increase community demand for JE vaccines, which can improve vaccination coverage. A 2012 survey of pig farmers in Nepal found that, although they are at high risk for JE, only 42 percent of the farmers had heard of JE, and none were vaccinated against it.<sup>10</sup> By continuing to improve JE awareness through education, the Nepal MOH aims to increase the reach and sustainability of JE vaccination to all those at risk.<sup>1</sup>

## A CASE FOR INVESTMENT

WHO recommends that JE vaccination should be integrated into national immunization schedules in all areas where JE is recognized as a public health priority.<sup>9</sup> Nepal demonstrates that, through commitment, resourcefulness, and creativity, it is possible to successfully implement a routine JE vaccination program despite logistical and financial challenges. The program has been highly successful and has added to the existing evidence that JE vaccines are safe, cost-effective, and efficacious, even in the most challenging settings.

JE vaccines have already saved lives and improved health for thousands of children of Nepal. By continuing to invest in these lifesaving vaccines, Nepal is on its way to making JE prevention history.

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