Is Japanese encephalitis control achievable by 2013?

For more on the **GAVI Alliance's new vaccine strategy** see **Editorial** *Lancet* 2008; **372:** 2

For the **study on JE by Solomon and colleagues** see *Clin Infect Dis* 2008; **47:** 458–468; DOI:10.1086/590008

For more on the **PATH JE project** see http://www.path.org/projects/japanese_encephalitis_project.php

For a **review of JE vaccines** see *Cochrane Database Syst Rev* 2007; **3:** CD004263; DOI:10.1002/14651858.CD004263.pub2

In June, the GAVI Alliance announced their decision to target seven key infectious diseases with high childhood mortality in the developing world. "In the next 5 years, GAVI Alliance will focus on supporting the use of new and underused vaccines to control cervical cancer, cholera, meningitis A, rabies, rubella, typhoid, and Japanese encephalitis (JE)", said Andrew Jones of the GAVI Alliance. The Alliance board meets in October to finalise details of their financial commitment and strategy.

Tom Solomon (University of Liverpool, UK) told *TLID* that "the decision to target JE is timely—it could save thousands of children from an early death and lifelong disability". JE, a mosquito-borne viral infection, affects around 50 000 people in Asia annually and is regarded as the leading global cause of viral encephalitis. Kaushik Bharati (National Institute of Immunology, New Delhi, India) points out that approximately 3 billion people live in JE endemic regions, with 70 million children born in affected countries each year. Solomon and colleagues published a study in July showing that 10% of children die during the acute stage of infection. At least half of the survivors are left with severe cognitive impairment, motor deficiencies, and paralysis. "Their development and quality of life is severely compromised, creating the need for life-long care and placing a substantial economic burden on their communities", said Solomon.

PATH

Children in India clutch their vaccination certificates during the 2006 Japanese encephalitis vaccination campaign

In the past, controlling JE in poor rural areas was difficult to achieve. Bharati points to inefficient vector control measures, the population explosion in the region, and an inadequate health infrastructure as underlying contributory factors. The lack of a widely accepted, safe vaccine has also been a major hindrance. "Because birds and pigs act as reservoirs and amplifying viral hosts, the virus cannot be eradicated: vaccination remains the most effective approach for preventing disease in human beings", explained David Beasley (University of Texas, Galveston, TX, USA).

An under-appreciation of disease burden caused by JE has meant that the potential value of routine childhood immunisation has been underestimated, Zhi-yi Xu (International Vaccine Institute, Seoul, South Korea) told *TLID*. "Clinically, JE is indistinguishable from other acute meningoencephalitis and the unavailability of diagnostic reagents has meant that, for example, Bali, Indonesia, had been considered a low-risk area until our research showed the opposite", he said. "The economic rationale for introducing immunisation programmes has often been obscured in endemic areas", agreed Karin Schiøler (University of Copenhagen, Denmark).

"The 70-year-old original JE vaccine was too expensive for public-health programmes and there were issues with adverse effects and manufacturing standards, but several new vaccines are now poised to enter the market", said John Wecker (PATH, Seattle, WA, USA). There are four main contenders; none have yet received the WHO prequalification GAVI requires before buying the vaccine for eligible countries, but some, if not all, manufacturers are expected to apply to WHO before 2011.

"The initial target group for the Intercell/Novartis vaccine is reported to be travellers and military personnel, but plans also include licensing and marketing it as a childhood vaccine in endemic countries", reported Schiøler. Successful phase III trials are being followed by a paediatric clinical trial in India in partnership with the Indian manufacturer Biological E, which is seen as a prelude to making it available in southeast Asia. "Other inactivated viral vaccines are being developed in Japan by Biken and Kaketsuken", added Beasley. The ChimeriVax-JE vaccine (Acambis/Sanofi Pasteur), a recombinant DNA vaccine, has completed phase III trials in adults and is now also undergoing a paediatric clinical trial.

The final option is a live-attenuated vaccine produced by the Chengdu Institute of Biological Products in China which, at less than US$0·50 per dose, is going to be substantially cheaper than the other products, making it an attractive option for consideration by GAVI. "At this point, we expect to support JE vaccines in the way we support other vaccines—with countries providing a small co-payment, depending on their income level, and GAVI covering the rest", said Jones. Xu points out that the Chengdu vaccine has been used for years in China, and, as a result of upgraded production and control standards, is now licensed in South Korea, Nepal, Thailand, and Sri Lanka. It has also been deployed in successful vaccine campaigns in India for the past 3 years, and "is expected to attain WHO prequalification approval by 2009", said Schiøler.

Wecker stresses that the public demand for the new JE vaccines in southeast Asia is likely to be high, noting that Uttar Pradesh, India, a state with one of the lowest routine immunisation coverage rates in the country, recorded a 99% turnout for JE vaccination in 2006. "To meet this demand, GAVI Alliance support for sustainable, routine vaccination programmes will be critically important", he concluded.

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