

# Vaccines on trial

One of the largest ever vaccine studies is under way in Kolkata. **Paroma Basu** uncovers the benefits, and difficulties, of inoculating 60,000 people against cholera and typhoid fever.

**F**amed for its poets and filmmakers, disgruntled Marxists and sleepy government clerks, Kolkata, a city of about 14 million people in northeastern India, may seem an unlikely setting for one of the largest clinical trials in the world.

In the poorest areas of this city, residents live in homes jammed together along winding sewage-littered pathways and rely on shared toilets and drinking water. Typhoid fever and cholera are endemic in India, and are chronic problems in Kolkata. Cholera, in particular, has a tenacious grip on the state of West Bengal, often called the 'homeland of cholera'.

The vaccine industry has been reluctant to commit resources to the development of vaccines for some of the world's poorest people. But a grant of US\$40 million from the Bill & Melinda Gates Foundation is helping to introduce affordable vaccines to cities such as Kolkata. The money has funded the five-year Diseases of the Most Impoverished (DOMI) Program, an initiative of the South Korea-based International Vaccine Institute (IVI).

DOMI is studying the social, economic and clinical effects of introducing vaccines into six other countries: Pakistan, Bangladesh, China, Indonesia, Vietnam and Thailand. Since 2000, it has launched two cholera studies, six projects investigating typhoid fever and another six exploring shigellosis, a common bacterial disease. The work is unprecedented, says John Clemens, the IVI's director, not only because of the project's size but also because it focuses on a demographic long ignored by drug companies, lawmakers and public-health officials.

In a unique research effort, 60,000 Kolkata slum-dwellers will participate this summer in phase III trials of an oral cholera vaccine. Last



A rhyming couplet written in Bengali invites Kolkata's residents to receive free vaccinations.

November, researchers injected the same population with a vaccine against typhoid fever.

The typhoid fever vaccine was developed at the US National Institutes of Health, and was donated by GlaxoSmithKline. The cholera vaccine is modelled on a widely available oral vaccine, Dukoral, which was developed in Sweden during the 1970s.

But at several dollars a dose, Dukoral is too expensive for most developing countries. Vietnamese scientists licensed the technology in the early 1990s and formulated a cheaper version at about 20 cents per dose.

With the IVI and Kolkata-based National Institute of Cholera and Enteric Diseases (NICED), Shantha Biotechnics, an Indian biotechnology company, is developing a local version of the Vietnamese vaccine and has procured regulatory clearances for the Kolkata trials. It has also secured the right to market the vaccine if it is approved, says Raman Rao, head of clinical research for Shantha.

Meanwhile, the roadblocks encountered during these trials in Kolkata are an example of the difficulties of carrying out such a programme, from political and religious tensions and bureaucratic delays to mistruths spreading like wildfire among the largely illiterate trial participants.

The project got off to a smooth start in 2002, with Kolkata epidemiologists performing a year-long surveillance study before identifying two slums that were particularly hard-hit by cholera and typhoid fever. But the next step was a bureaucratic nightmare, says Dipika Sur, deputy director of epidemiology at the NICED. The institute had to get an endless list of clearances from, among others, the national health ministry committee, local councillors, ethics

and human rights groups, Hindu priests, Muslim imams and community thugs.

But the clearances were easy compared with gaining the confidence of the study participants. During the typhoid vaccine trials, for instance, rumours spread that scientists were injecting cancer cells into people. Others believed they were being sterilized. "There was mass panic," Sur recalls.

About 65% of the targeted study group eventually gave their informed consent and received the typhoid jab. Sur thinks a big reason for this level of success was her tactic of employing 250 slum-dwellers to serve as the 'face' of the study, working as community health workers, field supervisors and sample collectors.

The strategy paid off largely because of staggeringly high unemployment levels in the slums. Montu Chandra Das, who was previously unemployed, now earns roughly US\$60 per month as a health worker. "It feels good to help others," he says.

Das goes door-to-door sending patients with persistent symptoms of diarrhoea or fever to one of seven 'health outposts', where patients receive free blood tests and medicines if diagnosed with cholera or typhoid.

"I like the way that the health workers come to check on us all the time," says Kamala Das, a 35-year old domestic helper who is taking part in the study. "Now we can see a doctor and be treated right away," adds another study member, Gopal Balmiki, a car driver who shares a room with 11 family members. "We know now that it's really important to keep the bathroom clean and drink unpolluted water."

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