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New analysis of old HIV vaccines finds potentially protective immune response

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Applying the benefit of hindsight, researchers at Duke Medicine have reanalyzed the findings of two historic pediatric HIV vaccine trials with encouraging results. The vaccines had in fact triggered an antibody response—now known to be associated with protection in adults—that was previously unrecognized in the infants studied in the 1990s.

Reporting online Aug. 28, 2014, in the *Journal of Infectious Diseases*, the Duke researchers relied on fresh insights that have been gleaned from a recent adult HIV vaccine trial in which the vaccine reduced the number of infections by about 30 percent.

That immune response, described by another Duke-led team last year, resulted from antibodies that attached to a specific region of the HIV virus's outer envelope, not from the broadly neutralizing antibodies that have long been considered necessary for widespread vaccine success.

But 20 years ago, when the two pediatric HIV vaccine trials were underway, the more specific antibody response was unknown, and therefore not measured.

Neither of the investigational vaccines advanced beyond early studies that tested whether they were safe for infants because analyses indicated they failed to elicit the broadly neutralizing antibodies considered the hallmark of success.

In the new analysis, the researchers retested the blood samples from the

earlier trials—one dubbed PACTG 230 and the other PACTG 326—to look for the recently identified antibody response associated with HIV protection.

The PACTG 230 trial began in 1993 enrolling infants born to mothers with HIV. The infants were randomly assigned to three groups: one receiving four doses of a VaxGen vaccine, another receiving a Chiron vaccine that included an adjuvant, and the third group getting a placebo treatment.

The PACTG 326 trial began in 1998, again testing a vaccine candidate among infants born to HIV-infected mothers. The babies were randomly assigned to receive either four doses of an ALVAC-HIV vaccine alone, or with a booster.

In the new analysis, the researchers found that infant HIV vaccination elicited the newly identified immune responses, particularly among the groups given the VaxGen and Chiron vaccines. At one year of age, 59 percent of the infants receiving VaxGen and 79 percent of those receiving the Chiron vaccine still showed this response. At two years of age, 28 percent of VaxGen and 56 percent of Chiron vaccinees continued to have detectable responses.

"It's encouraging to find that the vaccines had induced an antibody response that lasted so long," said lead author Genevieve G. Fouda, Ph.D., assistant professor of pediatrics at Duke. "In this population of infants, where the main goal is to prevent HIV transmission from mother-to-child during the period of breast feeding, inducing a two-year immunity would be long enough to be beneficial."

Fouda said developing a vaccine for use in infants remains an important pursuit, with an estimated 260,000 babies worldwide contracting the HIV virus from their mothers each year, many from breastfeeding. She

said additional studies should help determine whether the immune response identified in the early vaccine candidates actually provided protection against HIV infection, or whether it was merely a marker of protection.

"Scientists are trying to develop new vaccines that have an even better response than those we identified in the early trials," Fouda said. "Our work showed that vaccinated infants can make long-lasting, potentially protective antibody responses. It will be important to include infants in future HIV vaccine studies."

Provided by Duke University Medical Center