

# Genetic factors are linked to fever following smallpox vaccination

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New evidence supports the link between genetic factors and certain adverse events related to smallpox vaccination. The study, published in the July 15th issue of *The Journal of Infectious Diseases*, now available online, may have implications for predicting adverse events from other live vaccines.

Immunization against infectious agents has been one of the greatest successes of modern medicine, and the eradication of smallpox from the world is considered by some to be the crowning event of the 20th century. However, immunization with live virus particles, as in the smallpox vaccine, can sometimes cause reactions that range from fatigue to serious illness.

In recent studies testing the safety and potency of stored smallpox vaccine, which uses live vaccinia virus, some individuals developed fevers. The authors of the study, Samuel L. Stanley Jr., MD, and colleagues at Washington University, St. Louis University, and The Emmes Corporation, hypothesized that people who develop fever after vaccination may have genetically determined differences in their immune responses compared to those who do not. They studied 346 individuals who had participated in previous smallpox vaccination trials, 94 of whom developed fevers after vaccination. The authors analyzed 19 gene clusters (called haplotypes) linked to the body's response to viral infections.

The new study identified a total of eight haplotypes in four different

genes that were associated with altered susceptibility to fever after vaccination. It is the first study to show that fever after smallpox vaccination is associated with specific gene clusters in the interleukin-1 (IL-1) gene complex on chromosome 2 and the interleukin-18 gene on chromosome 11. The interleukins, and especially the IL-1 gene complex, are groups of molecules associated with inflammation and immune responses. The IL-1 gene complex, and especially the IL-1A gene, was the site most significantly associated with different risks of fever.

“Vaccines are the safest and most effective way to prevent a number of very important childhood and adult diseases,” Dr. Stanley remarked. “Our work is designed to identify ways we might make vaccines even more acceptable in the future by discovering ways to further reduce the chance of minor adverse events.”

In an accompanying editorial, James E. Crowe Jr., MD, of Vanderbilt University Medical Center, echoes Dr. Stanley’s sentiments that the findings represent an important preliminary step in understanding the variations in host responses to vaccines, and notes that further studies will need to replicate these findings, and to test other vaccines. Both Drs. Stanley and Crowe mention that the results may have important implications when it comes to the future goal of identifying individuals at risk for fever before they are given a specific vaccination. Crowe writes, “The long-term goal is to determine genetic features that could be determined prior to vaccination, allowing practitioners to modulate the vaccination plan according to risk. This type of practice, the goal of personalized predictive medicine, appears closer in feasibility than ever given the pace of genetic testing.”

Source: Infectious Diseases Society of America

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