

# Prophylactic paracetamol lowers the effect of childhood vaccines

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**F**ever is a frequent systemic adverse event following immunization, especially in infants and young children. Even if it is an element from the normal inflammatory process after vaccination, prophylactic antipyretic drugs are sometimes recommended to allay concerns of high fever and febrile convulsion. A team of researchers from the Czech Republic evaluated the effect of prophylactic administration of paracetamol at vaccination on infant febrile reaction rates and vaccine responses.

In two consecutive (primary and booster) randomised, controlled, open-label vaccination studies, 459 healthy infants were enrolled from ten centres in the Czech Republic. Children were randomly assigned to receive via suppository in three prophylactic paracetamol doses every 6–8 h (n=226) or no prophylactic paracetamol (n=233) after each vaccination with a ten-valent pneumococcal non-typeable *Haemophilus influenzae* protein D-conjugate vaccine (PHiD-CV) co-administered with the hexavalent diphtheria-tetanus-3-component acellular pertussis-hepatitis B-inactivated poliovirus types 1, 2, and 3-H influenzae type b (DTPa-HBV-IPV/Hib) and oral human rotavirus vaccines. The primary objective in both studies was the reduction in febrile reactions of 38°C or greater in the total vaccinated cohort. The second objective was assessment of immunogenicity in cohort.

The percentage of children with temperature of 38°C or higher was significantly lower in

the prophylactic paracetamol group (94/226 [42%] after primary vaccination and 64/178 [36%] after booster vaccination) than in the no prophylactic paracetamol group (154/233 [66%] after primary vaccination and 100/172 [58%] after booster vaccination). Vaccine immunogenicity was significantly lower in the prophylactic paracetamol group than in the no prophylactic paracetamol group after primary vaccination for all ten pneumococcal vaccine serotypes. The authors hypothesize that the effect could result from acetaminophen's preventing inflammation.

Even if over 95% of all children had seroprotective antibody levels and febrile reactions significantly decreased, the researchers concluded that "prophylactic administration of antipyretic drugs at the time of vaccination should not be routinely recommended since antibody responses to several vaccine antigens were reduced".

However, in a previous article (Expert Rev Vaccines, 2005 Jun) the authors underlined that "any fever after immunization may be caused by immunization or may coincide temporally as an indication of underlying disease, usually an infectious one. The time pattern of fever attributable to immunization has characteristic features depending on the vaccine used." Therefore, in the interpretation of the conclusions from the Lancet one has to have in mind the possible mentioned biases.

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*Comment on a paper:*

**R Prymula, CASiegrist, R Chlibek et al** – Effect of prophylactic paracetamol administration at time of vaccination on febrile reactions and antibody responses in children: two open-label, randomised controlled trials; *Lancet* 17 October 2009; Volume 374:9698; 1339-1350