

Hypotonic, hyporesponsive episode (HHE)

Hypotonic, hyporesponsive episode (HHE) is characterized by the sudden onset of reduced muscle tone, hyporesponsiveness and change in skin color (paleness or cyanosis). Other terms that have been used are “shock”, “shock like syndrome”, “collapse” and “collapse reaction”. While HHE has been documented after administration of diphtheria, tetanus, Hib and hepatitis B vaccines most reports of HHE follow vaccines containing pertussis components (DTP and DTaP). HHE has been observed more frequently following whole cell (DTP) than acellular pertussis (DTaP) containing vaccines. Incidence rates of HHE vary widely, from 36 to 250 and 4 to 140 per 100,000 doses for whole cell and acellular pertussis vaccines respectively. HHE has been observed more commonly after primary immunization series and particularly after the first dose.

The current case definition of HHE is:

- Level 1 of diagnostic certainty. The sudden onset of
 - a. Limpness (i.e. muscular hypotonia) AND
 - b. Reduced responsiveness (i.e. hyporesponsiveness) or unresponsiveness AND
 - c. Pallor or cyanosis.
- Level 2 of diagnostic certainty. The sudden onset of
 - a. Two of the three inclusion criteria defining Level 1.
- Level 3 of diagnostic certainty. The sudden onset of
 - a. Two of three inclusion criteria defining Level 1 and
 - b. The third criterion noticed to be absent.

The median time of onset of HHE after DTaP is within 1 hour with a range between 1 minute and 48 hours. Many children are irritable and febrile. They then become pale, limp, and unresponsive or hyporesponsive. Respirations are shallow and cyanosis is frequently noted. The median duration of HHE is 10 hours but can be as short as a one minute and as long as 14 days. Almost all reported cases, 86%, have sought medical care. The diagnosis is based on clinical findings and there are no laboratory investigations that are helpful.

HHE resolves without long term consequences. The ACIP lists HHE as a precaution (not a contraindication) against further doses of pertussis containing vaccines and most physicians do not administer further doses. However, in children who received further doses of pertussis containing vaccines there have been no recurrences.

References:

1. T. S. DuVernoy and M. M. Braun. Hypotonic-hyporesponsive episodes reported to the Vaccine Adverse Event Reporting System (VAERS), 1996-1998. *Pediatrics* 106 (4):E52, 2000.
2. J. Bonhoeffer, M. S. Gold, H. Heijbel, P. Vermeer, D. Blumberg, M. Braun, G. Souza-Brito, R. L. Davis, S. Halperin, U. Heininger, N. Khuri-Bulos, J. Menkes, and H. Nokleby. Hypotonic-Hyporesponsive Episode (HHE) as an adverse event following immunization: case definition and guidelines for data collection, analysis, and presentation. *Vaccine* 22 (5-6):563-568, 2004.