

Vaccine safety at the individual level – what have we learned?

Neal Halsey, John Hopkins Bloomberg School of Public Health, USA

Over interpretation of individual adverse events has led to false concerns, loss of public trust, and disruption of programs. Investigation of individual adverse events following vaccination is essential for post-licensure safety monitoring to maintain public trust in vaccines and to quickly identify new problems. Failure to investigate individual cases in a proper manner can leave the door open to inexperienced personnel making false assumptions of causal relationships that are not based upon appropriate scientific evidence.

Although some public health officials have stated that causality cannot be assessed from individual cases, all involved parties make judgments regarding the possible causal association about adverse events that occur following vaccines. Careful clinical investigation of individual cases can determine a) if the reported diagnosis is correct, b) the timing of the onset of disease, c) evidence for other causes of the illness, and d) underlying conditions that may have predisposed to the adverse events. Investigations sometimes reveal that adverse events reported after immunizations actually started prior to vaccine administration. Formal guidelines regarding the proper assessment of individual cases are being developed by the Clinical Immunization Safety Assessment (CISA) program through the Immunization Safety Office of CDC. A draft algorithm for assessing individual cases will be reviewed. When a causal relationship between the observed adverse event and the vaccine administered has been established from previous studies, the occurrence of such events within recognized time windows of increased risk is usually accepted as evidence that the adverse event was likely to have been caused by the vaccine in the absence of evidence of other possible causes. However, all cases should be investigated for evidence of other known causes because intercurrent infections and previously unrecognized underlying diseases that cause or contribute to adverse events can be identified. Appropriate specimens to help assess for other causes are often not collected in a timely manner. When there is no known causal relationship, assessment of individual cases can be problematic. Careful assessment of the rates of serious adverse events and comparison with expected rates can be helpful for reassuring the public that small numbers of cases are likely to occur by chance at all times after immunization. Affected individuals should be investigated for possible underlying factors that may have increased the risk of a serious adverse event, such as immune deficiency in patients who experience problems after live vaccines and pre-existing allergy to individual vaccine components in patients with hypersensitivity reactions. Special studies are indicated in some situations, such as hypersensitivity reactions, to determine if the participant can receive additional doses of vaccines, if indicated.

Committees or panels of experts to review selected adverse events for causality and provide advice regarding receipt of additional doses of vaccines are in place in some countries. Medical journals continue to publish individual case reports of unusual adverse events following vaccines with statements implying causal relationships when the evidence does not support causality. Standard guidelines are needed for medical journals for the review of case reports similar to the well accepted consortium guidelines for reporting clinical trials.