## TABLE 1-1 Summary of the Evidence For or Against a Determination of a Causal Relation [a]

| Vaccine and Adverse Event | Biologic Plausibility [b] | Case Reports, Case Series, and Uncontrolled Observational Studies | Controlled Observational Studies and Controlled Clinical Trials |
|---|---|---|---|
| *Diphtheria and Tetanus Toxoids* [c] | | | |
| Encephalopathy | Demonstrated | Indeterminate | Against (DT) No data (Td, T) |
| Infantile spasms [d] (DT only) | Theoretical only | No data | Against |
| Residual seizure disorders other than infantile spasms | Theoretical only | Indeterminate (DT, T) No data (Td) | No data |
| Demyelinating diseases of the central nervous system | Demonstrated | For | No data |
| Guillain-Barré syndrome | Demonstrated | For (T) Indeterminate (DT, Td) | No data |
| Mononeuropathy | Theoretical only | Indeterminate (T, Td)No data (DT) | No data |
| Brachial neuritis | Theoretical only | For (T) Indeterminate (Td) No data (DT) | No data |
| Arthritis | Theoretical only | Indeterminate | No data |
| Erythema multiforme | Theoretical only | Indeterminate (DT, Td) NO data (T) | No data |
| Anaphylaxis | Demonstrated | For (T) Indeterminate (DT, Td) | No data |
| Death from SIDS (DT only) [e] | Theoretical only | Indeterminate | Against |
| *Measles Vaccine* [f] | | | |
| Encephalopathy | Demonstrated | Indeterminate | Indeterminate |
| Subacute sclerosing panencephalitis | Demonstrated | Indeterminate | Indeterminate |
| Residual seizure disorder | Demonstrated | Indeterminate | No data |
| Sensorineural deafness | Theoretical only | Indeterminate (MMR) | No data |
| Optic neuritis | Demonstrated | Indeterminate | No data |
| Transverse myelitis | Demonstrated | Indeterminate | No data |
| Guillain-Barré syndrome | Demonstrated | Indeterminate | No data |
| Thrombocytopenia | Demonstrated | Indeterminate (measles) For (MMR) | Indeterminate (measles) No data (MMR) |
| Insulin-dependent diabetes mellitus | Theoretical only | Indeterminate | Indeterminate |
| Anaphylaxis | Theoretical only | For | No data |
| Death from vaccine-strain vital | Demonstrated | For | No data |

| | | | |
|---|---|---|---|
| infection [e] | | | |
| *Mumps Vaccine* [f] | | | |
| Encephalopathy | Demonstrated | Indeterminate | No data |
| Aseptic meningitis | Demonstrated | Indeterminate | No data |
| Residual seizure disorder | Theoretical only | No data | No data |
| Neuropathy | Theoretical only | No data | No data |
| Sensorineural deafness | Demonstrated | Indeterminate (MMR) | No data |
| Insulin-dependent diabetes mellitus | Demonstrated | Indeterminate | Indeterminate |
| Sterility | Demonstrated | No data | No data |
| Thrombocytopenia | Demonstrated | Indeterminate | No data |
| Anaphylaxis | Theoretical only | Indeterminate (MMR) | No data |
| *Polio Vaccine (OPV and IPV)* [g] | | | |
| Guillain-Barré syndrome | Demonstrated (OPV) Theoretical only (IPV) | For (OPV) Indeterminate (IPV) | For (OPV) No data (IPV) |
| Transverse myelitis | Demonstrated (OPV) Theoretical only (IPV) | Indeterminate (OPV) No data (IPV) | No data |
| Poliomyelitis (OPV only) | Demonstrate | For | No data |
| Thrombocytopenia (IPV) | Theoretical only | No data | No data |
| Anaphylaxis (IPV) | Theoretical only | No data | No data |
| Death from SIDS [e] | Theoretical only | Indeterminate | Indeterminate |
| Death from vaccine-strain vital infection, including from paralytic polio myelitis (OPV only) [e] | Demonstrated | For | No data |
| *Hepatitis B Vaccine* | | | |
| Guillain-Barré syndrome | Demonstrated | Indeterminate | No data |
| Demyelinating diseases of the central nervous system | Demonstrated | Indeterminate | No data |
| Arthritis | Demonstrated | Indeterminate | No data |
| Anaphylaxis | Theoretical only | For | No data |
| Death from SIDS [e] | Theoretical only | Indeterminate | No data |
| *Haemophilus influenzae* type b Vaccine | | | |
| Guillain-Barré syndrome | Theoretical only | Indeterminate | No data |
| Transverse myelitis | Theoretical only | Indeterminate | No data |

| | | | |
|---|---|---|---|
| Thrombocytopenia | Theoretical only | Indeterminate | Indeterminate |
| Susceptibility to early Hib disease [h] | Demonstrated | Indeterminate | For (PRP) Against (conjugated) |
| Anaphylaxis | Theoretical only | Indeterminate | No data |
| Death from SIDS [e] | Theoretical only | Indeterminate | No dam |

a Indeterminate indicates that there is evidence in this category, but the committee did not consider that, on the whole, it weighed either for or against a causal relation. *No data* indicates that the committee did not find data of tiffs type directly bearing on a causal relation between the vaccine and the adverse event.

b The committee considered all adverse events to be theoretically plausible and, therefore, classified plausibility in support of causality as either theoretical only or demonstrated. Demonstrated biologic plausibility refers to information on the known effects of the natural disease against which the vaccine is given and the results of animal experiments and in vitro studies.

c Unless noted otherwise, the classification for tetanus toxoid (T), diphtheria-tetanus toxoid for pediatric use (DT), and tetanus-diphtheria toxoid for adult use (Td) is the same. The committee was not charged with assessing monovalent diphtheria toxoid or the combined diphtheria and tetanus toxoids and pertussis vaccine (DPT). In Appendix A, see the Executive Summary of *Adverse Effects of Pertussis and Rubella Vaccines* for conclusions about DPT.

d Infantile spasms occur only in the age group that receives DT but not Td or T. A possible causal relation between infantile spasms and Td and T was not examined.

e In this table, the committee summarizes the data regarding the causal relation between the vaccine and only those deaths that are classified as sudden infant death syndrome (SIDS) or that are a consequence of vaccine-strain viral infection. SIDS occurs primarily in infants too young to receive tetanus and diphtheria toxoids for adult use, measles vaccine, mumps vaccine, or usually, tetanus toxoid. Therefore, a relation between these vaccines and SIDS was not assessed. If the evidence favors the acceptance of (or establishes) a causal relation between a vaccine and an adverse event, and if that adverse. event can be fatal, then in the committee's judgment the evidence favors the acceptance of (or establishes) a causal relation between the vaccine and death from the adverse event. Direct evidence regarding death in association with a potentially fatal adverse event that itself is causally related to the vaccine is limited to tetanus-diphtheria toxoid for adult use and Guillain-Barré syndrome, tetanus toxoid and anaphylaxis, and oral polio vaccine (OPV) and poliomyelitis. Direct evidence regarding death in association with a potentially fatal adverse event that itself is causally related to the vaccine is lacking for measles vaccine and anaphylaxis, MMR and anaphylaxis, OPV and Guillain-Barré syndrome, hepatitis B vaccine and anaphylaxis, and *Haemophilus influenzae* type b unconjugated PRP vaccine and early-onset *Haemophilus influenzae* type b disease in children age 18 months or older who receive their first Hib immunization with unconjugated PRP vaccine. See Chapter 10 for details, The data are indeterminate regarding the causal relation between the vaccine and causes of death other than those discussed above. Data regarding death as an adverse consequence of the vaccines under review are discussed in Chapter 10 rather than in the vaccine-specific chapters.

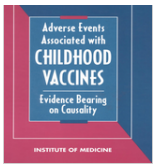
f The committee was charged with assessing the causal relation between several adverse events and measles vaccine or mumps vaccine. The committee was not charged with assessing monovalent rubella vaccine. In Appendix A, see the Executive Summary of *Adverse Effects of Pertussis and Rubella Vaccines* for conclusions regarding rubella vaccine. (MMR) indicates that the data derive exclusively from the multivalent preparation.

g OPV is oral polio vaccine; IPV is inactivated polio vaccine.

h The committee assessed data regarding the increased susceptibility to *Haemophilus influenzae* type b disease within 7 days of immunization with *Haemophilus influenzae* type b vaccine. For this adverse event only, the committee was able to separate the data regarding the unconjugated (PRP) vaccine from the data regarding the conjugated vaccines.

From: 1, Executive Summary

Adverse Events Associated with Childhood Vaccines: Evidence Bearing on Causality.




Institute of Medicine (US) Vaccine Safety Committee; Stratton KR, Howe CJ, Johnston RB Jr., editors.
Washington (DC): National Academies Press (US); 1994.