



Brachial Neuritis and Influenza Vaccination

Advisory Commission on Childhood Vaccines (ACCV)

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Health Systems Bureau (HSB)

Vision: Healthy Communities, Healthy People



ACCV's Request to HRSA



March 2, 2023

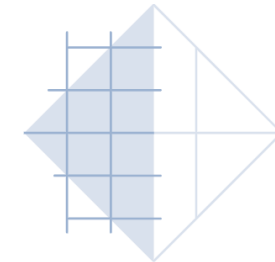
ACCV requested that HRSA provide background information to support a discussion of brachial neuritis and the influenza vaccine.

ACCV Guiding Principles for Recommending Changes to the Vaccine Injury Table (ACCV, 2006)

- ▶▶ The Table should be **scientifically and medically credible, AND**
- ▶▶ Where there is credible **scientific and medical evidence**, both to support and to reject a proposed change (addition or deletion), to the Table, the change should be made to the benefit of petitioners (whenever possible).

ACCV Guiding Principles for Recommending Changes to the Vaccine Injury Table (ACCV, 2006)

- ▶▶ To the extent that the Institute of Medicine (IOM) has studied the possible association between a vaccine and an adverse effect, the conclusions of the IOM should be considered by the ACCV and deemed credible. However, those conclusions should not limit the deliberations of the ACCV.



About IOM/NAM

Now known as the National Academy of Medicine (NAM)

- Founded in 1970 as the Institute of Medicine (IOM)

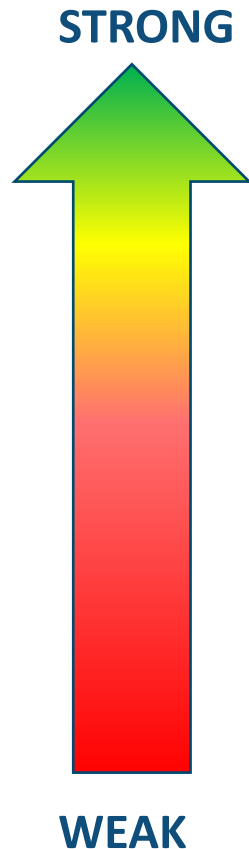
The original National Childhood Vaccine Injury Act of 1986 directed HHS to consult IOM to review scientific literature related to serious adverse events following immunization in children (§§ 312–313, P.L. 99-660, 100 Stat. 3743 (1986)).

In 2009, HRSA contracted IOM to review updated epidemiologic, clinical, and biological evidence regarding adverse events associated with vaccines covered by VICP.

HRSA presented a list of vaccine-related adverse events alleged in VICP petitions for IOM to review to determine vaccine causality.



ACCV Strength of Data Sources (ACCV, 2006)



- Clinical laboratory data
- Challenge/re-challenge/de-challenge data involving non-relapsing symptoms or diseases
- Controlled clinical trials
- Controlled observational studies such as cohort and case control studies
- Uncontrolled observational studies such as ecological studies
- Case series
- Data from passive surveillance systems
- Case reports
- Editorial articles on scientific presentations
- Non-peer reviewed publications

Strength of Scientific Evidence (UAB, 2022)

WEAK

- **Case studies and Opinion papers**
 - ✓ A report based on a single patient or subject

STRONG

- **Meta-Analysis and systematic reviews**
 - ✓ Aggregate and summarize multiple studies, through a systematic method, into a single report

Hierarchy of Scientific Evidence

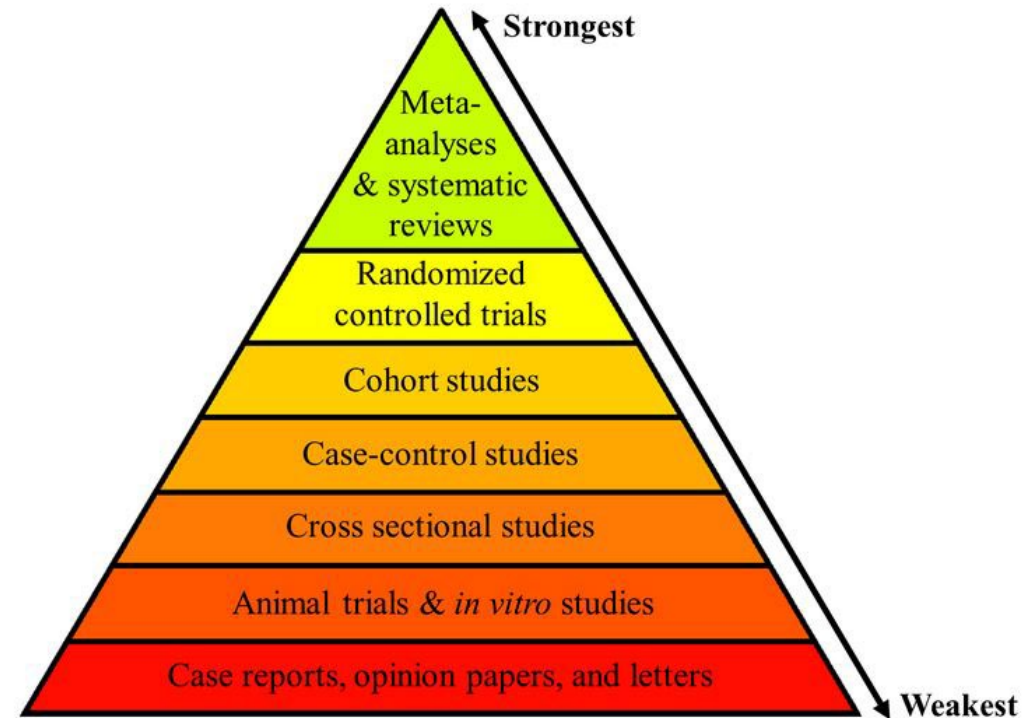


Figure 1. Evidence Pyramid from [UAB Library](#)

Injuries Not on the Vaccine Injury Table



Claims can be filed for injuries that are (1) not on the Table or (2) do not satisfy the Table's requirements

- Petitioner must show the vaccine caused the injury/condition by a preponderance of the evidence (more likely than not), and that the injury/condition did not have a more likely alternative cause



Claims can be compensated through concession, court decision, or negotiated settlement

- In a settlement, HHS does not endorse that the vaccine caused the injury

What is Brachial Neuritis? (Khalili, 2022)

- ▶▶ Also known as
 - Parsonage Turner Syndrome
 - Neuralgic Amyotrophy
 - Brachial Plexopathy
- ▶▶ A form of peripheral neuropathy that affects the nerves going to the chest, shoulder, arm, and hand (i.e., the brachial plexus)
- ▶▶ Incidence of 2-3 cases per 100,000 people per year
- ▶▶ Potential causes include trauma, toxins, neoplasms, radiation, viral and other infections, rheumatologic and autoimmune disorders, tetanus vaccine

Brachial Neuritis – Mechanism of Action

(Khalili, 2022)

▶▶ Exact mechanism **UNKNOWN**

▶▶ Theories include:

▶▶ Viruses directly affect the brachial plexus

▶▶ Immune response from an infectious agent affects the brachial plexus (autoimmune)

▶▶ Nerve biopsies show neovascularization, perineural thickening, and focal fiber loss suggesting ischemic changes that point to possible immune pathogenesis



Brachial Neuritis – Presentation (Khalili, 2022)



Fig. 2 Winged Scapula. (Hosey 2004)
from [Orthopedics](#)

- ▶▶ Deep, steady, often severe aching **PAIN** in the shoulder and upper arm
- ▶▶ **WEAKNESS** in affected upper extremity muscle groups
- ▶▶ Sensory loss
- ▶▶ Abnormal range of movement
- ▶▶ 80% of patients have a unilateral onset, and 60% involve the dominant side, 20% affect bilateral extremities onset

Brachial Neuritis – Presentation (Khalili, 2022)

- ▶▶ Involves two or more nerves affecting the muscles of the upper plexus
- ▶▶ Electromyography Nerve Conduction Studies (EMG/NCV) show:
 - ▶▶ abnormalities attributable to the nerves in the brachial plexus
 - ▶▶ must be distinguishable from other conditions attributable to nerve roots (i.e., cervical radiculopathies) and peripheral nerves (i.e., carpal tunnel syndrome)
- ▶▶ MRI may show signal abnormalities in the muscles of the shoulder girdle suggesting intramuscular denervation

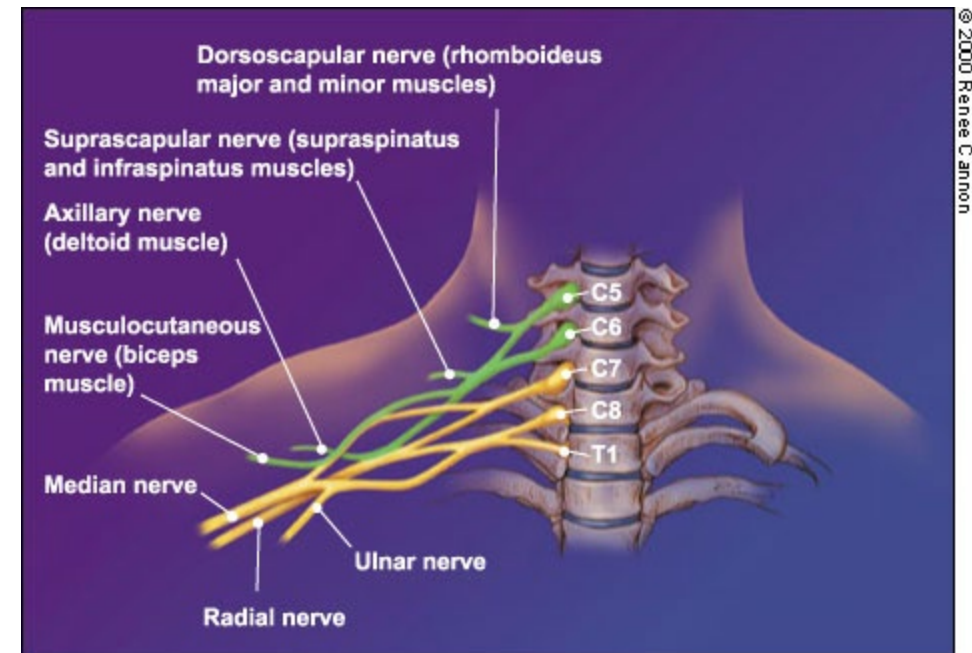


Fig. 3 Brachial Plexus from [AAFP](#)

Brachial Neuritis – Treatment and Prognosis (Khalili, 2022)



Conservative management

- Physical Therapy
- Glucocorticoids
- Analgesics



Recovery – months to years

- Usually full recovery with minimal deficits, if any

2012 IOM Report (National Academies Press, 2012)



Epidemiologic evidence – insufficient or absent to assess an association between influenza vaccine and brachial neuritis.

✓ No studies identified to evaluate risk



Mechanistic evidence – association between influenza vaccine and brachial neuritis is lacking.

✓ Two publications (Hansen, 2005; Wells, 1971) identified. No evidence provided beyond temporality



Causality conclusion – the evidence is **inadequate to accept or reject** a causal relationship between the influenza vaccine and brachial neuritis.

Observational study 2012-2015 (Hall, 2017)

Investigation of the safety of trivalent seasonal influenza vaccine available in Europe

- ✓ Reviewed medical records for 4,578 individuals during the study period
 - 1,011 vaccinations met the primary case definition, 16 adverse events
 - **NONE** of the adverse events were for brachial neuritis
- ✓ NO increased risk of brachial neuritis identified

	Risk Period (Preexposure Period) Days * Exposure = Day 0	Total Outcomes N	Outcomes in the Risk Period N, Observed to Expected (95% CI)	Incidence (95% CI) in the 6 Months Post Exposure
Neuritis (optic and brachial)	1-42 (-30 - 0)	0	0	—

Case Reports of Brachial Neuritis following Influenza Vaccination

Since the publication of the 2012 IOM report, there have been a few case reports:



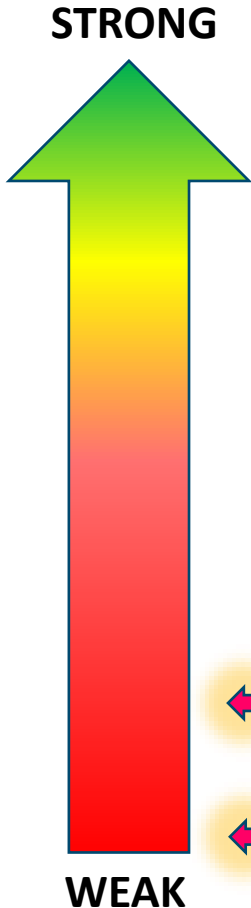
- 46-year-old woman developed left shoulder pain and weakness days after receiving influenza vaccine. No definitive association other than a temporal relationship (Shaikh, 2012).
- 85-year-old man complained of left shoulder pain and weakness 1 week after the influenza vaccine (Sinha, 2017).
- 29-year-old male presented with left shoulder pain and weakness after 2nd COVID-19 vaccine dose. Recovered, then symptoms recurred 6 months later after receiving influenza vaccine (Vanlecker, 2022).

Vaccine Adverse Event Reporting System Data – Brachial Neuritis & Influenza Vaccine Abstract (Shah, 2018)

- ▶▶ The objective was to determine the rate and characteristics of brachial plexopathy after influenza vaccination in adults in the U.S.A.
- ▶▶ 160 cases of brachial plexopathy identified from 1990 - 2017
 - Reported rate of new post-vaccination brachial plexopathy was 6 per year, within range expected in general population
 - Average onset (78% in 2 weeks, 10.75% 3 – 6 weeks) and distribution (21% > age 65) found to be different from non-plexopathy events and Guillain-Barré Syndrome after vaccination
- ▶▶ Authors concluded that although reporting rate for plexopathy post influenza vaccination is within range expected for general population, the distribution of cases suggest association may not be entirely coincidental
 - Recommended to continue monitoring of post vaccination plexopathy



Data Sources



Clinical laboratory data
 Challenge/re-challenge/de-challenge data involving non-relapsing symptoms or diseases
 Controlled clinical trials
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 Uncontrolled observational studies such as ecological studies
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- The current body of evidence evaluating an association between brachial neuritis and influenza vaccination is weak and does not contradict the conclusion of the IOM finding inadequate evidence to support or reject a causal relationship

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Factors to Consider in Discussing Whether Brachial Neuritis should be added to the Table for Influenza Vaccine



Etiology of Brachial Neuritis remains unknown

- Causal relationship has not been established with the Influenza vaccine



The last IOM report concluded that the evidence for an association between influenza vaccine and brachial neuritis is lacking



The strength of currently available data sources for the association between influenza vaccine and brachial neuritis is weak

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