Advisory Commission on Childhood Vaccines (ACCV)

Teleconference

March 8, 2024

Members Present

Albert Holloway, Jr. MD (2024)
Dana DeShon, DNP, APRN, CPNP-PC (2024)
Daniel Boyle (2024)
Timothy Thelen, JD (2024)
Divya Poduri (2026)
Ramon Rodriguez, III, JD, MD (2026)

Ex officio Members

Jonathon Duffy, MD, MPH, Centers for Disease Control and Prevention (CDC)
Claire Schuster, MPH, National Institutes of Health (NIH)
Sean Dade, MPA, Office of the Assistant Secretary for Health (OASH)
Jay Slater, MD, Food and Drug Administration (FDA)

Advisors

Heather Pearlman, Department of Justice (DOJ)
Lynn Ricciardella, Office of General Counsel (OGC)
Jocelyn McIntosh, United States Court of Federal Claims (CFC)

Division of Injury Compensation Programs (DICP), Health Resources and Services Administration (HRSA), U.S. Department of Health and Human Services (HHS)

CDR Reed Grimes, MD, MPH. Director, DICP, Chair, ACCV
Pita Gomez, Principal Staff Liaison, ACCV
Andrea Herzog, Program Analyst

Welcome and Chair Report, CDR Reed Grimes, MD, MPH, Director, DICP and Chair, ACCV

Commander Grimes called the meeting to order and welcomed everyone. Commander Grimes announced that all expected commissioners and ex officio members were present which constituted a quorum.

Public Comment on Agenda Items, CDR Reed Grimes, MD, MPH, Director, DICP and Chair, ACCV

Commander Grimes invited public comment on the meeting agenda and there were none.

Overview of Postmarketing Safety Monitoring, Meghna Alimchandani, MD, Deputy Director of Pharmacovigilance

Dr. Meghna Alamchandani from the FDA's Center for Biologics Evaluation and Research (CBER) provided an overview of post-marketing safety monitoring at the FDA, specifically from a CBER perspective. Dr. Alamchandani covered the organizational chart to orient attendees to where CBER fits within the agency and discussed FDA responsibilities during the product lifecycle, focusing on vaccine and therapeutics pharmacovigilance. Dr. Alamchandani explained passive and active surveillance, signal evaluation, and risk management processes, concluding with examples and a summary.

The organizational chart highlighted the different centers within the FDA, focusing on CBER, which co-manages Vaccine Adverse Event Reporting System (VAERS) with CDC. CBER is responsible for VAERS, while FDA Adverse Event Reporting System (FAERS) is managed by the FDA and Center for Drug Evaluation and Research (CDER). FAERS receives millions of reports, primarily for drugs regulated by CDER, but also for biologic products like cell and gene therapies regulated by CBER.

The Division of Pharmacovigilance within the Office of Biostatistics and Pharmacovigilance (OBPV), conducts post-marketing safety monitoring for all CBER-regulated products using both VAERS and FAERS. Dr. Alamchandani explained that product development begins years before a product reaches the market, starting in the pre-IND stages and continuing through clinical trial phases. The division is involved in reviewing the original licensing application and planning for post-marketing studies, emphasizing that product safety is critical throughout the product lifecycle.

FDA conducts post-marketing safety surveillance because clinical trials may not detect all safety issues. Clinical trials have limitations such as small sample sizes, limited observation periods, and exclusion criteria that often omit groups like pregnant women. Post-marketing surveillance is necessary to reveal interactions with comorbidities and ensure robust safety monitoring.

Pharmacovigilance, as defined by the World Health Organization, involves the detection, assessment, understanding, and prevention of adverse drug effects or other drug-related problems. The pharmacovigilance plan provided by the manufacturer during the review of the original licensing application includes safety specifications, identified risks, potential risks, and missing information. FDA reviews this assessment and may provide recommendations. Pharmacovigilance actions include routine pharmacovigilance, mandated by regulations, and post-marketing safety studies. These studies can be sponsor studies, targeted safety studies, or post-marketing commitments agreed upon between the manufacturer and FDA. FDA tracks the timelines for these studies, which are posted publicly.

Dr. Alamchandani also mentioned Risk Evaluation and Mitigation Strategies (REMS), which FDA can impose for certain products if necessary for benefits to outweigh risks. Few REMS programs exist within CBER, and none are for vaccines.

Dr. Alamchandani then discussed passive surveillance databases, specifically VAERS and FAERS. VAERS accepts reports from any source, including healthcare professionals, patients, parents, caregivers, vaccine manufacturers, and others. VAERS is co-managed by CDC and FDA, with data publicly available via CDC Wonder and downloadable datasets. FAERS is used by both CDER and CBER, with 96% of reports coming from manufacturers. The regulations for biologics, whether vaccines or therapeutics under Code of Federal Regulations (CFR) 600.80, dictate mandatory reporting by manufacturers.

Dr. Alimchandani provided an overview of post-marketing safety monitoring at the FDA from a CBER perspective. Dr. Alimchandani covered the organizational structure, FDA responsibilities during the product lifecycle, and the processes involved in pharmacovigilance. Dr. Alimchandani discussed both passive and active surveillance, signal evaluation, and risk management, concluding with examples and a summary.

Passive surveillance, as Dr. Alimchandani explained, involves spontaneous adverse event reports, which are voluntary and not solicited in a study. These reports lack denominator data and often result in underreporting since they rely on voluntary submissions from healthcare providers and the public. However, manufacturers are mandated to report serious and unlabeled adverse events within 15 days of becoming aware of them under regulations 600.80 and 314.80. Serious adverse events include death, hospitalization, life-threatening disability, congenital anomaly, or other medically important events.

Manufacturers also submit periodic safety reports to the FDA, which include an assessment based on both U.S. and foreign data. These reports are submitted quarterly for the first three years post-licensure and annually thereafter. Pharmacovigilance databases like VAERS and FAERS are integral to this process, serving as early warning systems for product safety. They accept all reports regardless of plausibility or clinical seriousness, and they can detect rare adverse events and generate hypotheses.

Dr. Alimchandani highlighted the strengths and limitations of adverse event reporting systems. Strengths include the ability to rapidly detect potential safety problems, detect rare adverse events, and gather data from diverse geographic locations. Limitations include missing or inaccurate data, under-reporting, stimulated reporting, lack of a control group, and difficulty in assessing causal associations. Additionally, product utilization data is essential for providing context for adverse events, though it has its own limitations.

Dr. Alimchandani then discussed active surveillance and post-marketing studies. The Biologics Effectiveness and Safety System (BEST)under CBER's umbrella is a key component of the FDA's active surveillance efforts. This system, also known as the CBER Sentinel Program, allows for robust post-market safety monitoring. Additionally, CDC's Vaccine Safety Datalink (VSD) and its data partners play a crucial role in active surveillance.

Dr. Alimchandani emphasized the importance of both passive and active surveillance in ensuring the safety of licensed products throughout their lifecycle. She underscored the FDA's commitment to continuous monitoring and evaluation of product safety to protect public health.

Dr. Alimchandani provided an in-depth presentation on post-marketing safety monitoring at the FDA from a CBER perspective. The presentation included an overview of the organizational structure, FDA responsibilities during the product lifecycle, and processes involved in pharmacovigilance, encompassing both passive and active surveillance, signal evaluation, and risk management. The discussion concluded with examples and a summary of key points.

The presentation concluded with an invitation for questions from the audience.

Commander Grimes thanked Dr. Alamchandani for her comprehensive review of post-marketing safety monitoring. Commander Grimes expressed appreciation for the detailed presentation and opened the floor for questions from the ACCV commissioners.

Dana DeShon began by commending Dr. Alamchandani's presentation and recalling the intussusception issues found with the rotavirus vaccine in the 1990s, which led to its removal from the market and subsequent rigorous testing of new vaccines. Dr. Alamchandani confirmed that there is always high vigilance for intussusception with rotavirus vaccines and thanked Dana DeShon for her comment.

Commander Grimes reiterated the robustness of the vaccine safety surveillance system in the U.S. and appreciated all the work that goes into passive and active surveillance. Dan Boyle noted that the presentation inspired confidence and referenced the previous day's discussion on vaccine hesitancy. Dan Boyle found the COVID-19 vaccine example from VAERS data particularly helpful and asked about any similar examples from V-safe.

Dr. Alamchandani explained that reports from V-safe are routed to VAERS and asked if any CDC colleagues could provide additional information. Dr. Duffy added that V-safe and VAERS are complementary systems, with V-safe sending periodic surveys and VAERS being open-ended for reporting any events.

Ray Rodriguez thanked Dr. Alamchandani and inquired about the extent of under-reporting in VAERS and whether there have been efforts to improve passive reporting systems. Dr. Alamchandani acknowledged that under-reporting cannot be quantified precisely but emphasized the complementary nature of various surveillance systems to catch safety signals.

Divya Podhuri asked about the communication of adverse effects to reduce vaccine hesitancy and whether doctors are required to inform patients about potential risks. Dr. Alamchandani highlighted the importance of transparent communication, CDC recommendations, and vaccine information statements to address public concerns and provide detailed information.
Dan Boyle followed up with questions about under-reporting, shifting baselines, and the complexities of tracking adverse events. He emphasized the importance of V-safe's methodical approach in prompting individuals to assess and report their situations. Dr. Alamchandani acknowledged these points and reiterated the value of multiple reporting and surveillance systems.

Dana DeShon concluded by mentioning the importance of healthcare providers using VAERS and giving information sheets to families, ensuring that they are informed about potential adverse effects and can report any unusual reactions.

Commander Grimes thanked everyone for their questions and comments, appreciating the engagement and insights shared during the discussion.

Epidemiology of Meningococcal Disease in the US and Updates on Meningococcal Vaccines, Sarah Schillie, MD, MPH, MBA

Captain Sarah Schillie spoke about the epidemiology of meningococcal disease in the United States and provided updates on meningococcal vaccines.

Globally, almost all meningococcal disease is caused by serogroups A, B, C, W, X, or Y, although only four of those serogroups circulate in the United States. The incidence of meningococcal disease in the United States from 1996 through 2022 was depicted, noting that the incidence started to decline before the introduction of the MenACWY vaccine in 2005. There has been an uptick in disease incidence in recent years.

The proportion of disease by serogroup from 2012 through 2021, predominantly pre-pandemic data, showed that serogroup B accounted for more than half of cases among adolescents. The proportion of disease caused by serogroup for 2020 through 2022 during the COVID pandemic was also shown, noting that the Y-axis scale on this slide differs from the previous slide.

The prevalence of meningococcal carriage by age in developed countries showed that carriage peaks in adolescents and young adults, with over 20 percent of that age group as carriers. While carriage rates can be high, disease remains rare because much fewer than 1 percent of people colonized with meningococcal bacteria develop the disease.

While most meningococcal disease cases are sporadic, outbreaks account for around 5 percent of cases in the United States. Outbreaks can occur either in organizations such as schools or in the community. Due to the rarity but seriousness of meningococcal disease, an outbreak can be declared with as few as two cases in an organization or an incidence above the baseline in a community. In recent years, serogroup B outbreaks among university students, serogroup C outbreaks among men who have sex with men, and outbreaks among people experiencing homelessness have accounted for a majority of outbreaks in the United States.

The meningococcal vaccine products available for use in the United States were summarized. There are two quadrivalent MenACWY products with trade names Menveo and MenQuadV. There are two MenB vaccines with trade names Trumenba and Bexsero. Additionally, there is one pentavalent MenABCWY vaccine with the trade name Pembrea. MenACWY vaccines target the serogroup-specific polysaccharide capsule of Neisseria meningitidis.

The first licensed quadrivalent MenACWY vaccines were polysaccharide-based and were poorly immunogenic, particularly in children under the age of two, unable to induce long-term

immunity because they triggered a T-cell independent response, generating predominantly IgM antibodies. The current MenACWY vaccines conjugate each serogroup-specific polysaccharide capsule to a carrier protein. This increases immunity by creating a T-cell dependent response, which leads to an IgG antibody response. The first conjugate MenACWY vaccine was licensed in the U.S. in 2005, and these conjugate vaccines have now completely replaced polysaccharide vaccines in the U.S.

The development of serogroup B vaccines has been difficult. The major challenge for serogroup B vaccine development was that, while the polysaccharide capsule of *Neisseria meningitidis* was used to make the MenACWY vaccines, the serogroup B capsule is poorly immunogenic in humans because it closely resembles a human neural cell antigen, causing safety concerns. Since the polysaccharide capsule antigen was not a good serogroup B vaccine candidate, attention turned to identifying protein antigens for a protein-based vaccine. However, serogroup B meningococcal strains are highly diverse, with variation in the sequence and expression of surface protein antigens, making it difficult to develop a universal serogroup B vaccine.

Extensive research identified some relatively more conserved protein antigens among serogroup B meningococcal strains, which were used to develop two MenB vaccines. Bexsero, or MenB4C, contains three protein components and outer membrane vesicles containing PorA, derived from the successful New Zealand outbreak strain vaccine, included to improve immunogenicity. The second MenB vaccine is Trumenba, or MenB-FHBP. Trumenba only contains two alleles of the FHBP protein. Since nearly every *Neisseria meningitis* isolate expresses FHBP, the manufacturer of Trumenba included just two FHBPs, representing both FHBP subfamilies, instead of including other antigens, which are less immunogenic or less universally present. Both subfamily A and subfamily B FHBPs were included because, while cross-protection is expected within each subfamily, it is not expected between subfamilies.

Although the antigens in the MenB vaccines were specifically chosen to protect against a wide range of serogroup B strains, variation in the antigen sequences and their expression levels in different strains mean that the MenB vaccines still do not protect against every MenB strain. On the other hand, because some of the proteins in the MenB vaccines are also found in meningococci of other serogroups and non-groupable meningococci, the MenB vaccines also have the potential to offer cross-protection against non-serogroup B strains.

Protection wanes over time following vaccination. For MenACWY vaccines, protection wanes between 3 and 8 years post-vaccination. Within 1 year of vaccination, vaccine effectiveness is 79%. Between 1 and 3 years post-vaccination, vaccine effectiveness is 69%. And between 3 and 8 years post-vaccination, vaccine effectiveness is 61%. For MenB vaccines, protection wanes 1 to 2 years following primary vaccination.

Captain Sarah Schillie discussed the vaccine schedule. All adolescents aged 11 through 18 years are routinely recommended for MenACWY vaccination with the first dose given at age 11 or 12 years and a booster dose at 16 years. MenACWY vaccination is also recommended for people at least 2 months old who are at increased risk for meningococcal disease, including people with specific medical conditions, such as complement deficiency, asplenia, HIV infection, as well as people who are at increased risk of exposure, such as microbiologists, persons in congregate

living settings, such as college freshmen and military recruits, and travelers to endemic areas. MenACWY vaccination is also recommended for people who are at increased risk during a meningococcal disease outbreak.

MenB vaccine is recommended for people 10 years and older at increased risk for meningococcal disease, which is somewhat narrower than the risk groups recommended for MenACWY vaccine. In addition, MenB vaccine is recommended based on shared clinical decision-making for adolescents and young adults aged 16 through 23 years to provide short-term protection from serogroup B disease. The shared clinical decision-making recommendation is intended to be flexible and informed by the characteristics, values, and preferences of the individual patient and the clinical discretion of the healthcare provider. This is unlike the MenACWY series, which is recommended for all adolescents.

Table 1 from the Child and Adolescent Immunization Schedule was referenced. The table summarizes the Advisory Committee on Immunization Practices (ACIP)'s vaccine recommendations by age, showing that MenACWY and MenB vaccines are listed in different rows. MenACWY has routine recommendations for adolescents aged 11 through 12 years.

Captain Schillie then discussed the dosing intervals. For healthy children and adolescents, ACIP recommends that the first dose should be administered at age 11 or 12 years and a booster dose at age 16 years, with the typical dosing interval being 4 through 5 years. Regarding catch-up vaccination, adolescents who receive their first dose at age 13 through 15 years should receive a single booster dose, preferably at age 16 through 18 years. The doses of MenACWY vaccine need to be separated by at least 8 weeks. Healthy adolescents who receive their first dose of MenACWY at or after age 16 years do not need a booster dose unless they become at increased risk for meningococcal disease.

Although routine vaccination is only recommended for adolescents age 11 through 18 years, MenACWY may be administered to persons age 19 through 21 years who have not received a dose after their 16th birthday. Note that at or after age 22 years, no booster dose is recommended for healthy persons. If MenACWY vaccine occurred at age 10 years, the routine vaccination at age 11 or 12 years should not be given. However, the child should still receive the booster dose at age 16 years. If MenACWY was administered before age 10 years, the child should follow the routine MenACWY vaccination schedule with the first dose at age 11 or 12 years and a booster dose at age 16 years.

For MenB vaccines in healthy persons, MenB vaccination is not routinely recommended for all adolescents. Instead, ACIP recommends MenB vaccination for healthy persons age 16 through 23 years based on shared clinical decision-making. If the decision is made to vaccinate, two doses are recommended, preferably at ages 16 through 18 years. Booster doses of MenB are not recommended for healthy persons. For Trumenba, the series is two doses separated by six months, and for Bexsero, it is two doses separated by one month. For Trumenba, if dose two is administered earlier than six months, a third dose needs to be administered at least four months after dose two.

Table 1 in the Adult Immunization Schedule was referenced. Both MenACWY and MenB vaccines are recommended for adults with risk factors, and MenB has the shared clinical decision-making recommendation for persons through 23 years of age. Recommendations for persons at increased risk are represented by the purple bars. Increased risk groups are listed in the far-left column, followed by the MenACWY recommended age of vaccination, if applicable, and MenB recommended age of vaccination, if applicable. For persons at increased risk, the number of doses and intervals vary based on risk condition, vaccine product, and patient age. Additional information can be found in the provided resources.

Booster doses are recommended in some situations. For MenACWY vaccine, for persons at increased risk younger than seven years, a booster dose is recommended three years after the primary series, and every five years thereafter. For persons seven years and older, a booster dose is recommended five years after the primary series, and every five years thereafter. For MenB vaccine, for persons at increased risk, a booster dose is recommended one year after the series, and every two to three years, as long as risk remains. During an outbreak, MenB vaccine may be administered at least six months after the series, if recommended by public health authorities.

MenACWY vaccine products are interchangeable. While it is preferable to administer subsequent doses with the same product used for the initial dose, this is not required for MenACWY vaccines. However, MenB vaccines are not interchangeable. All MenB vaccine products need to be from the same manufacturer. The pentavalent MenABCWY vaccine may be used when both MenACWY and MenB are indicated at the same visit. Use of the pentavalent vaccine should not supersede discussion of whether to administer MenB under shared clinical decision-making. However, if the pentavalent vaccine was inadvertently administered in lieu of MenACWY or MenB vaccine when only one was indicated, the dose can be considered valid.

Captain Schillie then spoke about vaccine coverage. The 2022 estimate of the percentage of 13-year-olds who had received at least one dose of MenACWY vaccine was 84.5%. Coverage of at least two doses, the full vaccine series, in 17-year-olds is 60.8%. MenB coverage is much lower, which is anticipated as the recommendations are not universal but rather based on shared clinical decision-making. The 2022 estimate of the percentage of 17-year-olds who received at least one dose of MenB vaccine was 29.4%. Coverage of at least two doses, the full vaccine series, in 17-year-olds was 11.9%.

Captain Schillie also discussed the safety of meningococcal vaccines. The MenACWY products contain no adjuvant, antibiotic, preservative, thimerosal, nor latex. Yeast is used in the manufacturing of MenVeo, and small amounts of formaldehyde are used in both products. BothMenB vaccine products contain an aluminum adjuvant to enhance the immune response. Bexsero contains the antibiotic kanamycin and Trumenba contains polysorbate 80 as a stabilizer. The products contain no thimerosal, yeast, or formaldehyde. Some Bexsero products may contain latex. In the Pentavalent product, Pembrea contains an aluminum adjuvant, polysorbate 80 as a stabilizer, and yeast is used in the manufacturing process.

Vaccination with MenACWY is contraindicated in persons known to have had a severe allergic reaction, such as an anaphylactic reaction, to a previous dose or to a vaccine component. Diphtheria toxoid is a component of MenVeo, and therefore, persons who have had a severe

allergic reaction to diphtheria toxoid should not receive MenVeo. Tetanus toxoid is a component of MenCWY, and therefore, persons who have had a severe allergic reaction to tetanus toxoid should not receive MenCWY. Like other vaccines, MenACWY should be deferred in persons with a moderate or severe acute illness until the condition has improved. MenACWY-CRM or MenVeo is a precaution in preterm infants aged less than 9 months due to concerns about apnea. Vaccination should be deferred unless the benefit of protection outweighs the risk for an adverse reaction. Adverse reactions after each type of MenACWY vaccine are similar. The most common from both clinical trials and post-licensure safety studies are injection site reactions, for example, pain and erythema, and systemic reactions, such as irritability, drowsiness, headache, myalgia, fatigue, and fever. Most adverse reactions are mild and moderate and resolve within three days.

Infection with MenB is contraindicated in persons known to have had a severe allergic reaction, such as an anaphylactic reaction, to a previous dose or to a vaccine component. MenB vaccine should be deferred in persons with moderate or severe acute illness until the condition has improved. Pregnancy is also a precaution for MenB vaccine. This vaccine should be deferred unless the benefit of protection outweighs the risk. Latex sensitivity is a precaution for some Bexsero products. The MenB vaccines can be reactogenic. Bexsero and Trumenba have similar adverse reactions after vaccination. The most common adverse reactions from both clinical trials and post-licensure safety studies are injection site reactions, such as pain, erythema, and induration, and systemic reactions, such as headache, myalgia, fatigue, arthralgia, and fever. Transient decreased mobility of the arm where Bexsero was injected has also been reported.

Early post-licensure surveillance raised the concern of a potential risk for Guillain-Barré syndrome (GBS) within six weeks of Menactra, but subsequent evaluations have not identified an increased risk for GBS after Menactra vaccination. It is important to note that Menactra is no longer available for use in the United States. An increased risk for Bell's palsy has been observed in adolescents within 84 days following vaccination when MenACWY-CRM, or Menveo, was co-administered with other vaccines. The increased risk was not observed when Menveo was administered alone. There are also reports of vaccine administration errors for Menveo related to failure to reconstitute the vaccine.

A theoretical risk exists for the development of Factor H autoantibodies following MenB-FHBP, or Trumenba, vaccination. Factor H autoantibodies are implicated in diseases such as atypical hemolytic uremic syndrome and C3 glomerulonephropathy. Trumenba contains Factor H-binding protein. However, the proportion of persons with a newly diagnosed autoimmune disease within six months was low and similar to unvaccinated controls. Transient decreased mobility of the arm was disproportionately reported for MenB-4C, or Bexsero, compared with other vaccines. Four cases of likely idiopathic nephrotic syndrome were identified in young children within one year following MenB-4C, or Bexsero, vaccination. The clinical significance of this is uncertain.

Regarding vaccination during pregnancy, no concerning events have been identified with MenACWY vaccination. As such, it is recommended if otherwise indicated. Generally, MenB vaccine is deferred during pregnancy. Vaccination-related syncope can be common in adolescents. 62% of VAERS syncope reports occurred among adolescents aged 11 through 18

years. Syncope-related falls can cause injury, for example, head injury. During a MenB vaccination campaign, there were 0.88 syncopal events per 1,000 vaccinated persons. Providers should consider observing patients for 15 minutes after vaccination, especially adolescents, and patients should be seated or lying down. Reducing the number of injections, for example, via combined MenACWY and MenB vaccines, may reduce the potential for syncope associated with vaccination among adolescents.

Captain Sarah Schillie discussed the impact of meningococcal vaccines. The incidence of disease following MenACWY vaccine implementation was shown, starting with serogroups ACWY. In the pre-vaccine era, MenACWY disease increased around ages 15 through 16. Following MenACWY vaccine implementation, the disease decreased dramatically, although there is still a peak at age 12. For serogroup B, it became the dominant cause of meningococcal disease in adolescents, although the incidence has decreased slightly since the pre-vaccine era.

Because the decline in meningococcal disease incidence began prior to the introduction of the vaccine, measuring the association between vaccination and disease incidence is challenging but has been modeled using surveillance data. Among adolescents aged 11 through 15 years, incidence decreased 16.3% during the pre-vaccine period and 27.8% during the post-primary dose period. Among adolescents aged 16 through 22 years, incidence decreased 10.6% during the post-primary dose period and 35.6% during the post-booster dose period. An estimated 222 cases of serogroup C, W, or Y disease were averted through vaccination of adolescents from 2006 through 2017.

Captain Schillie briefly discussed a hot topic in meningococcal disease prevention. ACIP is considering revising the adolescent meningococcal vaccine schedule to increase protection against meningitis B for college students, given the limited duration of protection from MenB vaccine. College students have a 3.5-fold higher risk of serogroup B disease than non-college students, with the highest incidence among 18 through 19-year-olds. Although meningococcal disease outbreaks account for only about 5% of cases in the U.S., 32% of the serogroup B cases among university students were associated with outbreaks. Higher risk is associated with students at a 4-year college as opposed to a 2-year college. Additional risk factors include being a first-year student, an on-campus resident, and participation in Greek life.

Neisseria meningitidis is genetically closely related to *Neisseria gonorrhea,* sharing about 80 to 90% sequence homology. As such, it is plausible for outer membrane vesicle meningitis B vaccines, such as Bexsero, to provide cross-protection against gonorrhea. An initial case-control study in New Zealand found an outer membrane vesicle MenB vaccine to be 31% effective against gonorrhea. Waning of vaccine effectiveness was noted, although the decrease in vaccine effectiveness was not significant between 2004-2009 and 2010-2014. Further studies in the United States and elsewhere have found similar effectiveness, about 30-40%. Considerations for gonorrhea protection may impact future ACIP deliberations regarding changes to the adolescent vaccine schedule.

In summary, meningococcal disease incidence is declining overall, although an uptick has been observed in recent years, and some persons remain at higher risk. Potential changes to vaccination policy will consider the changing epidemiology of meningococcal disease, the

duration of vaccine-induced protection, newly available pentavalent vaccines, and gonorrhea protection with MenB outer membrane vesicle-containing vaccines. Captain Schillie acknowledged those who contributed to the presentation and concluded by opening the floor for questions.

Ray Rodriguez asked about the recent uptick in meningitis cases and if it could be due to fewer people getting vaccinated. Captain Schillie noted that the exact reason for the uptick is unclear but could be related to changes in transmission patterns post-COVID-19. She also mentioned that decreased tobacco use and widespread antimicrobial use may have contributed to the historical decline in incidence.

Claire Schuster commented on a trial supported by NIH/National Institute of Allergy and Infectious Diseases (NIAID), looking at Bexsero for potential prevention against gonococcal infection, which is currently enrolling adults between 18 and 50. Captain Schillie expressed interest in following up on the trial.

Captain Schillie was also asked how the new pentavalent vaccine would be reflected in the schedules. She explained that it would be an option for providers and that there might be some advantages in reducing the number of injections for adolescents. The pentavalent vaccines are intended to be an option when both MenACWY and MenB are indicated at the same visit.

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) and Guillan-Barré Syndrome (GBS), James Sejvar, MD

Dr. Sejvar began with a disclaimer and proceeded to discuss Chronic Inflammatory Demyelinating Polyneuropathy (CIDP). CIDP is described as a chronic, ongoing, progressive, and/or relapsing disease of the peripheral nerves. Clinically, it presents as weakness, pain, and numbness in the limbs, as well as decreased or absent deep tendon reflexes. CIDP comes in two variants: typical CIDP and atypical variants. Typical CIDP is defined as chronically progressive, stepwise, periodically worsening, or relapsing and recurrent weakness in the proximal and distal muscles, along with sensory dysfunction in all extremities, evolving over eight weeks. This variant is also associated with decreased or absent deep tendon reflexes.

Atypical variants include those presenting predominantly distal weakness, asymmetrical weakness, pure motor without sensory involvement, or pure sensory without any weakness.

GBS shares many similarities with CIDP. GBS is an acute monophasic illness affecting the peripheral nerves, presenting as acute progressive weakness that eventually stops and either improves or plateaus. Similar to CIDP, GBS results in weakness, pain, and numbness in the limbs, and often affects cranial nerve-innervated muscles such as the eyes and face, along with decreased or absent reflexes. Variants of GBS include acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), Fisher syndrome, and other rare variants.

Dr. Sejvar illustrated the structure of a peripheral neuron, comparing it to an electrical wire, where the axon represents the wire and the myelin sheath represents the insulating cover. Damage to the myelin or the axon itself results in delayed or absent transmission of electrical signals through the nerve.

He discussed the case definitions for GBS and CIDP. The case definition for GBS, formulated by the Brighton Collaboration, includes acute onset of bilateral symmetric limb weakness, decreased or absent deep tendon reflexes, and a monophasic illness pattern with a maximum weakness period followed by a clinical plateau. Ancillary diagnostic tests, such as CSF examination and electrodiagnostic findings, increase diagnostic certainty.

The case definition for CIDP, established by the European Federation of Neurological Sciences and the Peripheral Nerve Society, includes inclusion criteria for typical CIDP and lists the variants, as well as supportive ancillary diagnostic tests.

Dr. Sejvar highlighted the similarities between GBS and CIDP and provided an overview of their pathogenesis. Both are considered immune-mediated diseases, involving an attack on self-proteins by the immune system, primarily targeting peripheral nerve myelin. The pathogenesis of CIDP is less understood compared to GBS, though certain antibodies, such as neurofascin-155 and neurofascin-186, as well as contactin-1, are involved in a small percentage of CIDP cases.

GBS is has been associated with antecedent infections or antigenic stimuli, such as some vaccines or toxins, leading to the formation of cross-reactive antibodies and autoreactive T cells that damage the myelin or axons. Anti-ganglioside antibodies, such as anti-GM1 and anti-GD1B, are strongly associated with GBS, particularly following *Campylobacter jejuni* infection due to molecular mimicry between the bacterium and ganglioside antibodies.

Dr. Sejvar concluded with an image illustrating the process by which proteins on the outer surface of Campylobacter induce the formation of IgG antibodies, which then react with gangliosides on the myelin sheath or axon, leading to immune-mediated damage.

Dr. James Sejvar presented on the topic of CIDP and its various forms. He explained that CIDP, or Chronic Inflammatory Demyelinating Polyneuropathy, is a chronic, ongoing, progressive, and/or relapsing disease of the peripheral nerves. Clinically, it presents as weakness, pain, and numbness in the limbs, as well as decreased or absent deep tendon reflexes. CIDP has two main variants: typical CIDP and atypical variants. Typical CIDP is characterized by chronically progressive, stepwise, periodically worsening, or relapsing and recurrent weakness in the proximal and distal muscles, along with sensory dysfunction in all extremities, evolving over eight weeks. Atypical variants include those presenting predominantly distal weakness, asymmetrical weakness, pure motor without sensory involvement, or pure sensory without any weakness.

Dr. Sejvar introduced a subtype called acute-onset CIDP (ACIDP), which has a rapid onset evolving over hours to days. It is particularly difficult to distinguish from GBS in its early phases. ACIDP is less common, representing less than 20% of CIDP cases. Features differentiating ACIDP from GBS include older age of onset, concurrent diabetes, and a greater

incidence of proprioceptive abnormalities. A primary distinguishing factor between ACIDP and the GBS subtype of AIDP is the progression period: ACIDP evolves over eight weeks or more, whereas AIDP reaches its peak within four weeks.

Dr. Sejvar compared the epidemiologic and clinical features of GBS and CIDP. Both illnesses increase in incidence with age and are more common in males. GBS has an incidence of one to two cases per 100,000 population per year, while CIDP's incidence ranges from 0.2 to 1.6 cases per 100,000 population per year, depending on the diagnostic criteria used. The prevalence of CIDP also varies widely. Geographic distribution shows higher rates of GBS in high-income Asia Pacific, North America, and lower rates in East Asia and South America. There is limited data on the geographic distribution of CIDP.

Dr. Sejvar discussed seasonality, noting that GBS has been observed to have seasonal peaks in winter or late summer/fall, while there is no data on seasonality for CIDP. He outlined risk factors for both illnesses, mentioning that GBS has been associated with underlying immunosuppression and certain surgeries. CIDP is more frequently found in people with type 2 diabetes, although diabetes as a risk factor for CIDP has not been well established.

Regarding vaccines, Dr. Sejvar explained that there is extensive data on GBS due to the 1976 H1N1 influenza vaccine incident, which showed a slight increase in GBS cases following vaccination. However, subsequent influenza vaccine formulations have shown a much lower risk. The Institute of Medicine has found no causal association between GBS and other vaccines. For CIDP, studies indicate a less than 1% risk of developing CIDP following vaccination.

Dr. Sejvar emphasized the strong causal association between *Campylobacter jejuni* infection and GBS, particularly the AIDP subtype, due to molecular mimicry. Other infections associated with GBS include varicella zoster, influenza, hepatitis E, and others. In contrast, CIDP has a lower incidence of antecedent respiratory or gastrointestinal illness, and there is no strong association with Campylobacter.

Dr. Sejvar highlighted the differences in the progression of GBS and CIDP. GBS presents acutely and reaches its peak within four weeks, followed by a plateau or recovery. CIDP develops over several weeks, months, or even years, progressing over eight weeks or more, with patterns of chronic progressive, stepwise, or relapsing progression, often with periods of stabilization.

Dr. James Sejvar emphasized the differences in the rate and strength of evidence regarding antecedent vaccines and infections preceding CIDP and GBS. For GBS, there is evidence suggesting a causal association between Campylobacter and AMAN. A temporal association exists between the 1976 influenza vaccine and GBS variants, though the specific variants were not identified during the investigation. There is also a loose temporal association between GBS and other vaccines and infections, including shingles, some influenza vaccines, mycoplasma, and hepatitis E infections. Overall, antecedent infection or vaccination is reported in about 70% of GBS cases, compared to about 9% for antecedent infections and about 1% for vaccinations in CIDP cases.

Dr. Sejvar discussed the progression of illness, a key factor in understanding the differences between GBS and CIDP. GBS presents acutely and evolves over hours to days, with symptoms typically progressing within one to two weeks. Most patients reach their clinical nadir within four weeks, followed by a plateau or recovery. In contrast, CIDP develops over several weeks, months, or even years, as a chronic autoimmune neuropathy progressing over eight weeks or more. CIDP has three temporal patterns: chronic progressive, stepwise, and relapsing, with possible periods of stabilization lasting years.

He briefly mentioned the electrodiagnostic criteria for diagnosing GBS and CIDP, highlighting the similarities in CSF findings. Both conditions are associated with albuminocytologic dissociation, characterized by elevated CSF protein with a normal white cell count. This finding appears in about 80% of AIDP patients by the second week of illness and about 90% of patients with all CIDP variants at some point. However, protein elevation is not specific to GBS or CIDP and can also be found in conditions such as diabetes and Charcot-Marie-Tooth disease.

Dr. Sejvar then compared the outcomes and treatments for GBS and CIDP. GBS can be severe, with reported mortality rates ranging from 1.9% to 5%, and about 30% of patients requiring intubation during their illness. Approximately 20% of GBS patients cannot walk unaided six months after onset. CIDP has a mortality rate between 1% and 11%, with 2% to 14% experiencing loss of ambulation at any point during their illness. Due to its chronic nature, CIDP results in more long-term morbidity. Treatment for GBS includes intravenous immunoglobulin (IVIG) or plasmapheresis, both equally effective, while steroids are not helpful and may be harmful. For CIDP, corticosteroids are the mainstay of treatment, along with IVIG and plasmapheresis in some cases. Some CIDP patients require ongoing higher potency immunotherapy to mitigate long-term disability.

In conclusion, Dr. Sejvar summarized that both CIDP and GBS are immune-mediated peripheral neuropathies, resulting in limb weakness, sensory deficits, and decreased reflexes. While they share similarities in clinical presentation and pathophysiology, they differ significantly in clinical course, progression, treatment, associated morbidity and mortality, and antecedent antigenic stimuli. GBS has strong associations with preceding infections and some vaccinations, whereas CIDP does not exhibit the same relationship.

Following the presentation, the floor was opened for questions. Dan Boyle thanked Dr. Sejvar for his in-depth presentation and highlighted the point about antecedent antigenic stimuli. Dan Boyle mentioned the relevance of studies on COVID-19 infection and vaccines in relation to GBS and CIDP. Dr. Sejvar responded that there has been significant focus on COVID-19 vaccines and natural infection to determine any increased risk of GBS or CIDP. He stated that, based on multiple studies, there is no strong signal suggesting an association between COVID-19 infection or currently available COVID-19 vaccines and GBS at levels comparable to the 1976 flu vaccine or Campylobacter infections.

Ray Rodriguez asked about the difficulties in diagnosing GBS variants versus CIDP variants, particularly distinguishing recurrent GBS from CIDP. Dr. Sejvar explained that while there are clinical features to help distinguish CIDP, such as older age and proprioceptive deficiencies, cranial neuropathies are common in GBS but rare in CIDP. Recurrent GBS is uncommon, and

relapses are more indicative of CIDP, which is pathophysiologically and epidemiologically distinct from GBS.

The discussion highlighted the common misconception that CIDP is a chronic version of GBS. Dr. Sejvar's presentation clarified that CIDP and GBS are distinct entities with different clinical courses and treatments.

Future Agenda Items/New Business

Commander Grimes took the floor and stated that the next item on the agenda was future agenda items and new business. He mentioned that there would be a National Academy of Medicine causality assessment focusing on shoulder injuries associated with intramuscular vaccination, expected to be completed by the end of March or early April. Commander Grimes noted the possibility of an ad hoc ACCV meeting before the next scheduled meeting in September 2024 to brief members on the findings. He advised the commission members to be on the lookout for emails regarding this potential meeting.

Commander Grimes then opened the floor for questions or comments about this topic. Ray Rodriguez raised his hand and inquired whether the anticipated report would be forwarded to the commission in advance for review prior to the proposed ad hoc meeting. Commander Grimes confirmed that the findings would be publicly available and shared with the commission beforehand. He added that there would likely be an hour to an hour and a half session to present and discuss the findings, providing an opportunity for questions.

After addressing Ray Rodriguez's question, Commander Grimes asked if there were any other comments or questions on that topic before moving to the next agenda item. Seeing none, he proceeded to discuss future topics for ACCV meetings. He mentioned that during the previous day's discussion, it was highlighted that the ACCV's duties include surveying federal, state, and local programs related to gathering information on injuries associated with the administration of childhood vaccines. Commander Grimes noted the excellent presentation from FDA colleagues that covered this topic in the federal space and expressed interest in having additional content on surveying these systems in future talks.

Commander Grimes then asked if there were other topics the commission would like to discuss at the next meeting. Seeing no hands raised, he mentioned that there would likely be an opportunity to bring up additional topics at the ad hoc meeting if it formalizes. He then moved on to the next agenda item related to brachial neuritis and influenza vaccination.

Commander Grimes reminded the commission of the presentation they received in September 2023 about the current state of evidence regarding brachial neuritis and influenza vaccination. He noted that while references and reports had been shared with the commission and questions were addressed, additional references had been shared by another commission member. Commander Grimes then opened the floor for discussion and invited Dan Boyle to share his thoughts, given that he had originally footnoted references in questions prior to the last meeting.

Dan Boyle appreciated the process and noted that Dr. Sejvar's presentation earlier fit well with the issues at hand. He mentioned that a vote was taken at the last meeting not to petition the secretary to add brachial neuritis to the vaccine injury table for the influenza vaccine. He highlighted that the vote was taken before commissioners had seen the additional references he had provided. Dan Boyle expressed concern that they might not have had a quorum present when the vote was taken, as the written minutes indicated four votes. He left it to the commission to address this procedural issue and expressed interest in any comments or responses to the references he cited or those submitted since the last meeting.

Commander Grimes stated that according to the charter, a quorum for the purposes of a meeting is five members. He mentioned that they had received guidance indicating that the quorum number extends to ex officio members as well. Therefore, while there may have only been four voting members, a quorum can still be met by including additional ex officio members. From a technical perspective, Commander Grimes confirmed there was a quorum at the time, despite only four votes being cast. He then addressed the content and decision regarding brachial neuritis and influenza vaccination.

Commander Grimes invited Dana DeShon to provide additional information or perspectives on the matter, particularly regarding the additional resources she had provided for the commission to review. Dana DeShon acknowledged the process and mentioned that Dan Boyle had presented multiple questions to members and sought responses to those questions. She asked for clarification on how to proceed, whether she should state the questions and her responses or if Dan Boyle should present them.

Dan Boyle clarified that during the previous meeting, there was confusion about the references in the footnotes of his questions. He believed the commission had already voted at that point, and it was noted that the discussion would continue at the current meeting.

Commander Grimes confirmed that the questions submitted on the topic of brachial neuritis and influenza vaccination were read and responded to at the last meeting. However, the references cited in the footnotes were not shared at that time, which were subsequently shared before the current meeting along with additional references from Dana DeShon. Commander Grimes asked if this was an accurate representation, to which Dan Boyle agreed.

Dan Boyle elaborated that his footnoted references were in response to the September 2023 presentation. He added detail to the discussion prompted by the presentation, focusing on issues such as the incidence rate and prevalence of brachial neuritis. Dan Boyle highlighted the importance of considering advances in diagnostic techniques over the past decade and the potential need to add brachial neuritis to the vaccine injury table. He also noted that brachial neuritis might be the most common injury compensated for influenza vaccine.

Commander Grimes then took the floor to further the discussion. He asked if any ACCV Commission members had any discussion points or comments on the additional references shared by Dan Boyle and Dana DeShon. He encouraged the commission members to raise any specific content-related points for discussion with fellow commission members.

Commander Grimes stated that the commission members had an opportunity to review the additional references and discuss any new insights or changes in perspective that might arise from these references. He reiterated the importance of ensuring that all relevant data and perspectives were considered in making informed decisions.

Dan Boyle expressed his gratitude for the opportunity to serve on the commission and for the platform to share his questions and input. Commander Grimes thanked Dan Boyle for his contributions and opened the floor for any further comments or discussion points from the commission members regarding the topic of brachial neuritis and influenza vaccination.

Dana DeShon reviewed the references provided by both herself and Dan Boyle. She addressed one of the questions concerning brachial neuritis, which Dan had stated might be 30 to 50 times more prevalent according to epidemiological reports before 2015. Dana DeShon mentioned a Korean study that looked at VAERS and the European Consortium on Vaccine Surveillance, emphasizing that VAERS is a reporting system and should not be used to establish causality. If there is a trend, an alert is triggered for further investigation. The Korean study noted strong seasonality with a peak in summer. The Vaccine Safety Data League and mobile apps like v-safe were recommended for surveillance in Korea to resolve public mistrust in vaccines.

Dana DeShon pointed out that the confidence interval of the Korean study's prediction was 95%, but not adjusted for multiple testing, indicating the need for further research to determine significance levels. She also referred to a Netherlands study in a primary care setting, where incidence of brachial neuritis was found to be higher after practitioners received training on its diagnosis, which could have led to ascertainment bias. The study did not mention the cause of brachial neuritis except for one patient with hereditary neurologic aminopathy.

Dana DeShon referenced a 2021 study she had provided, which concluded a 1 in 130,000 association between shoulder inflammatory conditions like bursitis and vaccination without confirmatory experimental evidence supporting an immune-mediated inflammatory response to vaccine antigens. She noted that new diagnostic tools such as high-resolution ultrasounds have implications for studying the mechanisms and plausibility of causation of brachial neuritis by influenza vaccine.

The standard care for brachial neuritis involves conservative treatment for three months, with tests like ultrasound and MRI used if it persists. Dana DeShon emphasized that brachial neuritis is poorly understood and difficult to diagnose. She cited studies indicating that more than half of patients describe a recent event such as infection, strenuous exercise, surgery, trauma, vaccination, rheumatological disease, hepatitis C infection, or childbirth. Genetic links were also noted, with hereditary factors assumed to play a role.

Dana DeShon addressed another of Dan Boyle's questions, noting that over 30 cases of brachial neuritis following influenza vaccination were reported and settled between November 2019 and February 2023. However, compensation does not imply causation. She referenced a 2020 study that found most shoulder injury claims were related to influenza vaccine injections administered too high on the arm. Proper injection technique and anatomical landmarks are crucial to avoid such injuries.

Regarding brachial neuritis listed in the vaccine injury table for vaccines containing tetanus toxoid, Dana DeShon mentioned a 1994 IOM report that found evidence favoring a causal relationship between tetanus toxoid and brachial neuritis. She questioned whether this precedent could be applied to influenza vaccines, given the absence of controlled epidemiological studies. Dana DeShon cited multiple references and studies that did not find a clear link between vaccines and brachial neuritis, including a 2018 study and a 2020 systematic review.

Dana DeShon concluded by discussing the feasibility of reviewing the biological mechanisms of brachial neuritis and influenza vaccines by the Clinical Immunization Safety Assessment (CISA) Network or another entity. She emphasized that compensation for vaccine injuries does not mean the vaccine caused the injury and noted that many studies have not found a clear link between vaccines and brachial neuritis.

Public Comment

Commander Grimes stated that the next agenda item was for public comment.

Zoom users were instructed to use the reaction button to raise their hand if they wanted to make a public comment, and those dialed into the meeting could press star 9 to be unmuted. She noted the first comment from Theresa Wrangham and proceeded to unmute her.

Theresa Wrangham introduced herself, noting that she is the Executive Director of the National Vaccine Information Center. She acknowledged her previous comment and reiterated that the organization has represented and been a voice for the vaccine-injured, worked with Congress, and sat on the committee over its 40-year existence. Theresa Wrangham appreciated the discussion on GBS versus CIDP and highlighted Commissioner Boyle's concerns around brachial neuritis, emphasizing the importance of considering individual susceptibility even without a public health signal.

She stressed that the purpose of the VICP was to ensure that injuries, even without a public health signal, were taken seriously. Theresa Wrangham mentioned the Institute of Medicine's presentation on individual susceptibility, which indicated that personal and familial histories could predispose one to injury. She emphasized the importance of public access to discussions, citations, and references mentioned during the meeting to maintain transparency.

Theresa Wrangham noted that GBS was added to the vaccine injury table for the flu shot. She questioned why similar data mining was not conducted for brachial neuritis. Theresa concluded by reiterating the need for more public and transparent discussions, supported by presentations to the commission, to ensure the public could follow and understand the deliberations.

Other public comments were solicited. Commander Grimes moved to the next item on the agenda, which was the adjournment of the March 8, 2024, meeting. He asked if there was a motion to adjourn.

Tim Thelen requested a discussion about the transparency comment regarding making communications public before entertaining the motion to adjourn. Commander Grimes agreed and asked Tim Thelen to raise his question directly.

Tim Thelen suggested making both Dan Boyle's and Dana DeShon's emails part of the public record for this meeting since they were discussed at length[1]. He clarified that there was no intent to have a private conversation and moved to add them to the record.

Commander Grimes acknowledged the motion to add the questions, responses, and references to the record and asked if the motion was seconded. Ray Rodriguez seconded the motion.

Commander Grimes proceeded with a vote to include the notes in the public record:

- Dan Boyle: Yay
- Dana DeShon: Yay
- Albert Holloway: Yay (indicated by a thumbs up)
- Tim Thielen: Yay
- Stevia Paduri: Yay
- Ray Rodriguez: Yay

The motion was unanimously approved, and Commander Grimes expressed appreciation for bringing this forward and thanked the comments that generated it.

Commander Grimes noticed Dr. Holloway's raised hand and invited him to speak. However, there was no response. Tim Thelen then moved to adjourn the meeting, which was seconded by another member.

Commander Grimes conducted a quick vote on the motion to adjourn:

- Dan Boyle: Aye
- Dana DeShon: Yes
- Albert Holloway: Thumbs up (indicating a yes)
- Tim Thelen: Yay
- Stevia Paduri: Yes
- Ray Rodriguez: Aye

Commander Grimes announced that the motion to adjourn was unanimously approved. He thanked all the presenters and participants for their contributions and participation in the meeting. He then officially adjourned the 129th ACCV meeting and wished everyone a great weekend.

Commander Grimes invited a motion to adjourn. On motion duly made and seconded, the meeting was adjourned.

[1] Email communications have been added to the end of meeting minutes.

From: [redacted]
To: [redacted]
Subject: [EXTERNAL] Re: ACCV Meeting March 7, 2024
Date: Sunday, March 3, 2024 3:03:33 PM

Hi Annie,
In response to Mr. Boyle's questions I also have some articles addressing his questions (6 of them). Would you like the copy of those articles to disperse as well or offer that information at the meeting?
Thank you!
Dana DeShon
Here are the references:
1. Chang L, Meng Y, Janosczyk H, Landolfi V and Talbot HK. Safety and Immunogenicity of High-Dose Quadrivalent Influenza Vaccine in Adults ≥65 years of Age: A Phase 3 Randomized Clinical Trial. Vaccine. 2019;37(39):5825-5834.ISSN: 0264-410X.
2. Dudley MZ, Halsey NA, Omer SB, et al. The State of Vaccine Safety Science: Systematic Reviews of the Evidence. The Lancet Infectious Diseases. 2020;20(5):e80-e89.ISSN: 14733099.
3. . Dudley MZ, et al. "Do Vaccines Cause Brachial Neuritis?" The Clinician's Vaccine Safety Resource Guide: Optimizing Prevention of Vaccine-Preventable Diseases Across the Lifespan. Edited by Matthew Z. Dudley, et al. Springer International Publishing, Cham, 2018a
4. Gonzalez AI, Kortlever JTP, Moore MG and Ring DC. Influenza Vaccination is Not Associated with Increased Number of Visits for Shoulder Pain. Clinical Orthopaedics and Related Research®. 2020;478(10)ISSN: 0009-921X.
5. Hesse EM, Atanasoff S, Hibbs BF, et al. Shoulder Injury Related to Vaccine Administration (SIRVA): Petitioner Claims to the National Vaccine Injury Compensation Program, 2010–2016. Vaccine. 2020;38(5):1076-1083.ISSN: 0264-410X.
6. Woo EJ, Moro PL, Cano M and Jankosky C. Postmarketing Safety Surveillance of Trivalent Recombinant Influenza Vaccine: Reports to the Vaccine Adverse Event Reporting System. Vaccine. 2017;35(42):5618-5621.ISSN: 0264-410X.

On Wed, Feb 7, 2024 at 1:40 PM [redacted] (HRSA) <[redacted]> wrote:

> Hello ACCV Members,
>
> As discussed during the September 8, 2023 meeting, attached are the questions submitted by Dan Boyle. As requested, we have included the articles that he cited in his questions for your review. Thank you, and we look forward to seeing everyone on March 7, 2024. Please be on the lookout for our Meeting Books, which should be sent out shortly before our next meeting.
>
> [redacted]
> Division of Injury Compensation Programs
> Health Systems Bureau
> [redacted]
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Sign up for email updates

From: [redacted]
To: [redacted]
Subject: [EXTERNAL] Re: ACCV Meeting March 7, 2024
Date: Sunday, March 3, 2024 3:41:28 PM

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sorry- one more article reference.
MacMahon A, Nayar SK and Srikumaran U. What do we Know about Shoulder Injury Related to Vaccine Administration? an Updated Systematic Review. Clinical Orthopaedics and Related Research. 2022;480(7):1241-1250.PMCID: PMC9191332. ISSN: 1528-1132; 0009-921X; 0009-921X.
Dana

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> [redacted]
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Questions for September 2023 ACCV meeting on Brachial Neuritis and Influenza Vaccination

Dan Boyle

Question: Brachial Neuritis from all causes may be 30 to 50 times more prevalent than epidemiological reports indicated previous to 2015, and the incidence may be increasing.[1] If this condition is not being identified, including for those who develop it after a vaccination, what implications does this have for evaluating VAERS data, and use of VSD and other sources of surveillance that have been used to find signals of adverse effects of brachial neuritis from any vaccine?

Question: Since the 2012 IOM report it appears that newer diagnostic tools such as high-resolution ultrasound are being used to diagnose brachial neuritis.[2] What implications do use of these tools have for studying the mechanisms and plausibility of causation of brachial neuritis by influenza vaccine?

Question: Between 11/16/2019 and 2/15/2023 there have been over 30 cases reported to have had adjudicated settlements for brachial neuritis following influenza vaccine[3]. Notwithstanding that "Being awarded compensation for a petition does not necessarily mean that the vaccine caused the alleged injury"[4], would it be reasonable to assume that these NVIC settled cases were

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1 van Alfen N, van Eijk JJ, Ennik T, Flynn SO, Nobacht IE, Groothuis JT, Pillen S, van de Laar FA. Incidence of neuralgic amyotrophy (Parsonage Turner syndrome) in a primary care setting--a prospective cohort study. PLoS One. 2015 May 27;10(5):e0128361. doi: 10.1371/journal.pone.0128361. PMID: 26016482; PMCID: PMC4445915

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4445915/

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And,

Huh K, Kim YE, Radnaabaatar M, Lee DH, Kim DW, Shin SA, Jung J. Estimating Baseline Incidence of Conditions Potentially Associated with Vaccine Adverse Events: a Call for Surveillance System Using the Korean National Health Insurance Claims Data. J Korean Med Sci. 2021 Mar 8;36(9):e67. doi: 10.3346/jkms.2021.36.e67. PMID: 33686812; PMCID: PMC7940120.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7940120/

2 Gstoettner C, Mayer JA, Rassam S, Hruby LA, Salminger S, Sturma A, Aman M, Harhaus L, Platzgummer H, Aszmann OC. Neuralgic amyotrophy: a paradigm shift in diagnosis and treatment. J Neurol Neurosurg Psychiatry. 2020 Aug;91(8):879-888. doi: 10.1136/jnnp-2020-323164. Epub 2020 Jun 2. PMID: 32487526.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4445915/

And,

Cignetti NE, Cox RS, Baute V, McGhee MB, van Alfen N, Strakowski JA, Boon AJ, Norbury JW, Cartwright MS. A standardized ultrasound approach in neuralgic amyotrophy. Muscle Nerve. 2023 Jan;67(1):3-11. doi: 10.1002/mus.27705. Epub 2022 Aug 30. PMID: 36040106; PMCID: PMC10087170.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10087170/

3 https://www.hrsa.gov/advisory-committees/vaccines/meetings

well documented and, if considered a case series, could add to the biologic plausibility that influenza vaccines could cause brachial neuritis?

Question: Brachial Neuritis is listed in the Vaccine Injury Table for vaccines containing tetanus toxoid. In the 1994 IOM report looking at Tetanus Toxoid they found that "The evidence favors acceptance of a causal relation between tetanus toxoid and brachial neuritis... the mechanisms of brachial neuritis are not well understood, there is biologic plausibility that vaccines could cause an allergic or hypersensitivity reaction that manifests as brachial neuritis. This provides reasonably good, although sparse, evidence that brachial neuritis can occur in relation to tetanus toxoid, although controlled epidemiologic studies designed to look at this relation do not exist."[5] Is this a precedent for a standard that could be used to look at brachial neuritis and influenza vaccines using case reports alone in the absence of controlled epidemiologic studies"?

Question: The 2011 Report, *National Vaccine Advisory Committee White Paper On The United States Vaccine Safety System*[6] stated: "Targeted clinical research into biological mechanisms of AEFI [Adverse Event Following Immunization] is essential. One locus of this work is the Clinical Immunization Safety Assessment Network (CISA)." Would a review of biological mechanisms of brachial neuritis and influenza vaccines by CISA or other entity be feasible and warranted to study this question given the number of cases of brachial neuritis following influenza vaccine that are being compensated?

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4 https://www.hrsa.gov/vaccine-compensation/data

5 Institute of Medicine (US) Vaccine Safety Committee; Stratton KR, Howe CJ, Johnston RB Jr., editors. Adverse Events Associated with Childhood Vaccines: Evidence Bearing on Causality. Washington (DC): National Academies Press (US); 1994. 5, Diphtheria and Tetanus Toxoids. Available from:

https://www.ncbi.nlm.nih.gov/books/NBK236292/

6 https://www.hhs.gov/sites/default/files/NVAC-White Paper-Vaccine-Safety-System.pdf