Vaccine Safety Quarterly (VSQ) | Spring 2021

Brighton Collaboration 2.0

Frederick Varricchio, PhD, MD - *Editor in Chief*

New Brighton Collaboration Case Definitions & Guidelines for Data Collection, Analysis, and Presentation of Immunization Safety Data and Case Definition Companion Guides

The SPEAC team is developing case definitions and guidelines for data collection, analysis, and presentation of immunization safety data for each adverse event of special interest (AESI) in the SPEAC Priority List of COVID-19 Adverse Events of Special Interest. New Case Definition Companion Guides are also being developed.

Case definitions

Case definitions and guidelines for data collection, analysis, and presentation of immunization safety data use the Brighton Collaboration format to provide a consensus case definition with defined levels of diagnostic certainty that can be utilized by clinicians and scientists for the evaluation of adverse events following immunization.

Companion guides

Case definition companion guides collate Brighton Collaboration resources (risk factors, background rates, ICD9/10-CM and MedDRA codes), tools (data abstraction and interpretation form, tabular summary of key case definition criteria and algorithm for level of certainty determination, pictorial level of certainty algorithm) and guidance (real time investigation, data collection, analysis and presentation) into a single document. These can be used to guide real time and retrospective investigation of adverse events, the latter reviewing and interpreting key medical record data.

Case definitions, companion guides and pharmacovigilance

An urgent global need to control the SARS-CoV-2 pandemic accelerated development of vaccines to protect against COVID-19 disease. While the new generation vaccine platforms such as viral vector and mRNA technologies already existed with varying degrees of clinical experience the greater challenge was to expedite the clinical and regulatory assessment processes. This was achieved by conducting vaccine development stages concurrently instead of sequentially, and with thousands of people who were willing to participate in phase I, II and III clinical trials of the new vaccines. Several COVID-19 vaccines have been granted emergency-use authorization. The subsequent rapid mass vaccination rollouts across ethnically and geographically diverse populations brings the importance of real-time safety surveillance of COVID-19 vaccination to identify rare adverse events following immunization (AEFIs), and particularly AESIs, during the post-authorization period to the fore.

Harmonization of AEFI and AESI reporting is essential, not only at the country level but also at the global level

Detection of rare AEFIs and AESIs not only requires data from very large numbers of vaccine recipients but also relies on data being comparable. Use of the Brighton Collaboration case definitions and guidelines can assist clinicians to conduct

standardized assessment and reporting, and standardized MedDRA/ICD-9/10-CM coding. When potential safety signals require urgent investigation, prior reports of similar or the same AEFI/AESI can be identified in and compared across multiple databases, such as VigiBase, the Vaccine Adverse Event Reporting System (VAERS), EudraVigilance and the Yellow Card scheme.

Causality assessment needs to consider event risk factors and background rates

Harmonized AEFI/AESI reporting can assist with causality assessments but cannot be used in isolation. Knowledge of event risk factors and the occurrence of the event in the population without exposure to the vaccine (background rate) is critical. When assessing potential safety signals, clinicians and scientists need to assess whether the event could be biologically or medically associated with the vaccination and assess how often the event is occurring in the vaccine exposed population compared with the background rate.

Use of the tools in the case definition companion guides can inform event risk factors and methodologies that use administrative data for the identification of AEFI/AESI background rates and pharmacovigilance risk assessments.

Future challenges

Identification of potential safety signals, such as the reports of atypical thromboembolic/thrombocytopenic events in Europe, require a rapid and thorough response from the scientific community to ensure vaccine recipient safety and to maintain global confidence in vaccination. They will face additional challenges when the rare and possibly unique syndromic events require development of new diagnostic criteria and are not captured with the existing codes nor covered by the existing case definitions.

Where to find case definitions and companion guides

New, pre-publication, case definitions and guidelines and the case definition companion guides are available on the Brighton Collaboration case definitions webpage.

Case definitions for Vaccine-Associated Enhanced Disease, Multisystem Inflammatory Syndrome in Children and Adults (MIS-C/A) and Acute Respiratory Distress Syndrome (ARDS) have been developed since October 2020. Earlier case definitions have been published in Vaccine.

Case definition companion guides for the Anaphylaxis, Acute Disseminated Encephalomyelitis (ADEM), Acute Encephalitis, Acute Myelitis, Aseptic Meningitis, Facial Nerve Palsy, Generalized Convulsion, Guillain Barre and Miller Fisher Syndromes, and Thrombocytopenia case definitions have been developed since November 2020.

Karin Batty

The Immunisation Advisory Centre
University of Auckland

Helen Petousis-Harris

University of Auckland

Member, Brighton Collaboration Science Board

COVID-19

Over 100,000 citations coded COVID-19 are listed in PubMed. Many appear to be from China but from many other countries as well. This is a remarkable achievement in one year. The signs, symptoms, course, and sequelae of this disease are still evolving and probably will continue to do so for some time. This does not include any possible relevant entries in the preprint servers. There are also numerous webinars some sponsored by the AMA. One issue of the Journal of American Medical Association had 6 articles on COVID-19 and dermatology, cardiology, etc. For the nonspecialist, Carlos del Rio has 15 articles summarizing some part of the COVID-19 story. Johns Hopkins University maintains a COVID-19 dashboard which provides a daily global update for 30 countries. A recent paper attempts to describe COVID-19 as a multisystem disease.

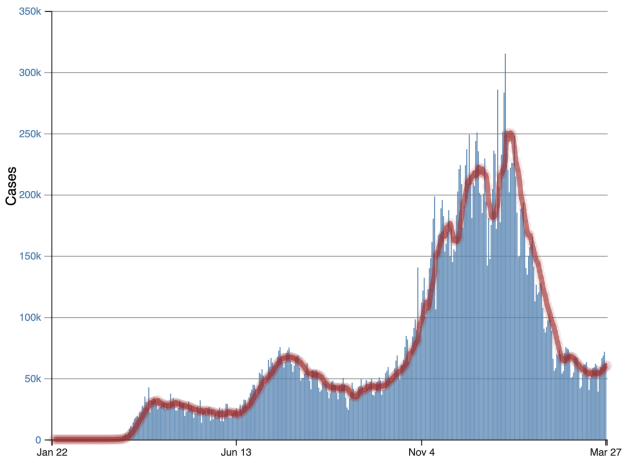
In terms of pathophysiology, the virus first binds ACE ll (angiotensin converting enzyme) receptors in the nasopharynx. This receptor is present in many organs including the endothelium. It can cause total destruction of the lung but actually affects multiple organ systems. Longer term effects include fatigue and somnolence, which affect about ⅓ of survivors, so called long haulers. Frequent cardiac effects have been reported and coagulopathy has been reported. For the generalist, an article on pathophysiology, transmission, diagnosis and treatment was recently published. A chronology of disease has been proposed. A review of autopsy findings is also available.

A “new AE” COVID-19 related inflammatory multisystem disorder has been reported and is similar to Kawasaki disease. Its status is currently being discussed. One very important issue still unanswered is how long antibodies to Covid-19 will persist (Emerg Infect Dis. 2020 Nov). Some 157,000 variants of COVID-19 have been characterized. A Swiss-Spanish group has used this information to track virus spread across Europe.

Mid-December a more contagious mutant was found in the UK. This mutant has already been found in several other countries. Other mutants are South Africa and Brazil which also are now widespread. Other so far more localized mutants such as California are being followed. Initial information is that the current vaccines will give effective protection against these mutants except the South African. Autoantibodies have been found in some cases and it has been proposed that they could account for some long term symptoms and coagulopathy.

WHO has issued a first report of the world's overall response to COVID-19. This report documents failures at every turn. And the U.S. Congress shows, unintentionally, masks work.

The New York Times continues to publish COVID-19 case counts as well as vaccine administration efforts in the US. There are also detailed diagrams of the COVID-19 genome and mutants Coronavirus variant tracker



Daily Trends in Number of COVID-19 Cases in the United States Reported to CDC

Treatment

Remdesivir has been approved for use in certain cases; however, its effect appears to be modest. Banlanivimab, a monoclonal antibody that blocks attachment of the virus to the ACE2 receptor, recently received emergency approval. It will be available through state health departments. It is noteworthy that Francis Collins, the NIH director, convened a meeting quickly in April 2010 to discuss drug therapy of COVID-19. This meeting brought together government scientists, regulators, FDA and drug industry leaders. They identified 170 compounds of potential interest.

The first report of screening known drugs for use against COVID-19 has appeared. An advantage to this approach is that much is known, positive and negative, about each compound. This method led to the first useful drug for AIDS, azidothymidine (AZT). However, to date COVID-19 drug therapy is still focused on Remdesivir. Articles attesting to the lack of efficacy of hydroxychloroquine continue to appear. The NYTimes maintains a report on progress in drug development Coronavirus drug and treatment The FDA has just announced a dedicated reporting system for Covid-19 therapeutics AE.

Of general interest is a story about how one biotech company rapidly turned significant attention and effort toward developing a COVID-19 treatment, Regeneron. Their product has received emergency FDA approval and is being used. It is a unique double antibody drug which acts by attaching to COVID-19 virus particles and thereby reducing viral load. Continuing this approach, a group of protein chemists is trying to develop molecules that would be even more efficacious. Another novel idea which has appeared is a bifunctional compound used as nasal spray which would prevent virus from attaching to the ACE2 receptor. But so far the search for treatment has been disappointing. A trial of convalescent serum in the emergency room was halted recently for lack of efficacy.

COVID-19 vaccine

The first successful vaccine trials have been completed. BioNTech-Pfizer (PB for short) and Moderna vaccines press releases claim about 95% success. First reports of actual use of these vaccines have a similar efficacy with 2 doses. A negative is that the PB requires extreme cold for storage and transport. They both use a novel messenger RNA (mRNA) platform. A third vaccine, Johnson and Johnson-Janssen has recently been approved and is already being used and reported 70-90% success. This vaccine uses a viral vector platform has advantages in stability and cost and only requires one dose. Partiality because of the mutants that have appeared, 2nd generation vaccines are already in progress. One goal is to develop a vaccine with broader efficacy. The FDA has already announced that 2nd generation will not require the usual large trials. Instead it may be possible to follow some immunological markers in a few hundred people for example. Actually about 8 vaccines are currently on the world market. This includes vaccines from Russia, China and India. A Cuban vaccine is in an advanced state of development. The New York Times maintains a list of the status of the 70 odd vaccines in development. About 6 different platforms are being tried. Merck has stopped development of 2 vaccines because of poor efficacy. The Astra-Zenica vaccine used in Europe has recently been stopped in several countries because of possible thrombogenesis, currently resolved. In the US questions have been raised about the integrity of the clinical trial, also resolved currently. There may be other changes in vaccine trials in the future because of experiences during this pandemic.

Since initial supplies of vaccine are still limited, discussions continue concerning priority of distribution. Furthermore, more worldwide distribution is being addressed by the COVAX

program. As of mid February an estimated 130 countries had not received 1 dose.

There has been much discussion about how a vaccine should be efficiently and fairly distributed. On December 1, 2020, U.S. CDC Advisory Committee on Immunization Practices (ACIP) met and advised that healthcare workers (~20 million) and nursing home residents (~3 million) have first priority and other groups according to risk. However, final decisions remain with individual states.

Some groundwork and planning for distribution were done in anticipation of the availability of the vaccine arrival but initial distributions did not go smoothly. Allergic reactions have appeared as an AE concern since mass vaccinations began. Most individuals were female and had a history of severe allergic reactions. A recent publication reports 66 known anaphylactic reactions cases involving both vaccines and compares them.

Brighton Collaboration has been involved along with CEPI in developing a list of possible AEFIs that may be associated with a COVID-19 vaccine. One concern is the potential for enhanced disease. This is theoretical for COVID-19 but has been seen with SARS and MERS-CoV vaccines in animal models. A guideline for Coagulopathy will be available in 3-4 months.

There have been numerous articles in the press about people, even military, who say that they do not want to be among the first to get the vaccine. Apparently, this is because of a feeling that a vaccine may be rushed to market. But about 100 million doses have been administered in the US. And 3 ex-presidents as well as the president and Anthony Fauci have been vaccinated publicly. It will be interesting to try to gauge the effect of that. Peter Marks, director of CBER-FDA, has stated that in his experience as an oncologist confidence is best achieved from a relationship with a physician. It is known that a trusted intermediary can have a powerful effect. China and Russia have vaccines and both are reported to be exporting to other nations.

Little is known about these products, The unprecedented speed in developing these vaccines is undoubtedly due largely to the use of new platforms Barring unforeseen problems, these approaches will soon be used for other vaccines and drugs.

COVID-19 testing

With little public notice there have been a series of improvements in virus testing. Now there's even a test that can be used at home. While speed usually compromises accuracy, each has its advantages. Now these tests must be evaluated as to how they perform with the Covid-19 mutant.

COVID-19 Vaccine Data Resources

Brighton Collaboration has assembled a COVID-19 vaccine safety resource. Topics include regulatory approvals, risk management plans, usage recommendations ,adverse events and databases. This resource is intended for public use by anyone who is interested in COVID-19 vaccine details.

Comments and additional sources may be sent to varricchio@comcast.net.

In general, CDC and MMWR are good sources. The FDA's Vaccine AE Reporting System (VAERS) database is available to the public.

VACCINE MISINFORMATION

Discussion continues concerning how to deal with vaccine misinformation and increase public confidence. Dubé outlined approaches to improving communication to the public and reviewed materials available -in Canada. They made specific suggestions for improvement such as: 1) targeting an audience and establishing trust, 2) providing balanced information, risks and benefits, 3) giving facts first before myths, 4) using visual aids, and 5) testing materials first. The CDC has 1 page "tip sheet" on frequent vaccine questions and responses. These are available in bulk Should physicians be encouraged to keep some in their waiting areas. A London anthropologist, Heidi Larsen thinks she knows how to deal with false information and build trust. She studies rumors and is founder of the Vaccine Confidence Project. Also see, "the science of changing someone's mind". Duke university medical school has added a course. The US Covid-19 relief law contains funds to work on the effort. Robert Kennedy has been a prominent vaccine doubter. His granddaughter, a physician, has publicly rebutted his position.

In recognition of the critical importance of COVID-19 vaccines and the need to understand their safety, the CONSIDER (**CO**vid-19 vacci**N**e **S**afety quest**I**ons an**D** h**E**althcare p**R**oviders) working group (WG) was created in September 2020. The CONSIDER WG aims to provide clear, comprehensive answers to questions pertaining to COVID-19 vaccine safety prior to, and during the vaccines roll out to 1) facilitate scientific discussion between stakeholders, including front line health workers with potential vaccine recipients and 2) increase comprehension and transparency of information to facilitate acceptance and uptake. As more questions come to the group's attention or more information becomes available, including on AEFI (from COVID-19 vaccine clinical trials and early experience with vaccine introduction in countries), the answers are being updated and new answers posted on https://canvax.ca/covid-19-vaccine-questions-and-answers-healthcare-providers and are cross-referenced on other sites, including on WHO's Vaccine Safety Network (VSN).

The UN has just announced an effort to make reliable COVID-19 information available to everyone called "Verified". It enables volunteers from around the world to share information. The theory is to enable social organization, people providing information to friends, family, and social contacts. More recently WHO has announced a collaboration with Wikipedia which is known to be frequently consulted by the public for health information. The WHO will make its information available for posting. The WHO also maintains a list of credible vaccine information sources, the Vaccine Safety Network (VSN). This contains primarily government sources but Brighton has just been included. Scientific American recently had an article on COVID-19 myths that won't go away. Most of these are familiar to us.

The new director CDC, Rochelle Walensky, has commented that these days most "scientific" information passes by Twitter. Therefore, responsible sources must Twitter too. She plans to make herself more publicly visible.

JOURNAL CLUB

In collaboration with the International Society for Pharmacoepidemiology (ISPE) Special Interest Group (SIG) on Vaccines, the Brighton Collaboration is pleased to continue the Vaccine Safety Journal Club. Members of both organizations are invited to review and discuss the latest research on vaccine safety, from epidemiological methods to qualitative research. The journal club will take place quarterly during SIG meetings via Webex, and will be co-hosted by SIG Chair Cathy Panozzo, Harvard and

BC member Nadja Vielot, University of North Carolina.

The next journal club will be held **April 7, 2021 at 9:00am EDT**. Jennifer Gerber will lead a discussion of "BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting" by Dagan et al. This article estimates the efficacy of the Pfizer-BioNTech COVID-19 vaccine following a mass vaccination campaign in Israel, supplementing clinical trial data with real-world data from over 1 million vaccinated individuals.

To join the discussion, please complete this Google Form and we will include you on the mailing list.

History

The man who named syphilis

(from Hektoen International)

One of the great names in medical history, Girolamo Fracastoro appears in the National Gallery painting by Titian in full regalia. We owe him the name syphilis, derived from his poem (1530) Syphilis sive morbus gallicus ("Syphilis or The French Disease") in which a shepherd boy named Syphilus was punished by Apollo with a horrible disease that could be treated with mercury. Perhaps brought to Europe by the crew of Christopher Columbus, it spread to Italy by the invading French troops and was accordingly named morbus gallicus or the French disease. Some scholars have speculated that Titian may have painted the portrait in exchange for himself being treated for syphilis.

Fracastorius was a polymath, physician, poet, and scholar. Descended from a patrician Veronese family, he was born there around 1476–1478. He studied literature, mathematics, astronomy, geography, philosophy and medicine at the academy in Padua, where immediately after receiving his degree in 1502 he became instructor in logic. In 1509 he returned to Verona, where he dedicated himself to his studies and developed a private medical practice, treating patients from all over Italy. Though interested in politics, he never held public office, but became widely known for his erudition and competence in liberal arts, philosophy, natural sciences, and medicine. His work De Contagione (1546) contains the first scientific suggestion that epidemic diseases could be transmitted by contagion caused by a different type of rapidly multiplying minute body. He speculated they were transmitted either by direct contact or through the air or by material such as soiled clothes or linen, which he called fomites. He also gave the first description for typhus.

Appointed in 1545 as physician to the Council of Trent, he influenced the transfer of the Council from Trent to Bologna because of the danger of plague. He suffered a fatal stroke in 1553 and was buried in Verona, where a statue in his honor was erected in 1555.

LITERATURE

There are about 2400 citations per year in PubMed coded Vaccine Safety. This is increasing by about 200 per month. I have selected a few which may be of general interest.

1. A review of using traditional Chinese medicine and small molecules to treat COVID-19

J Med Chem. 2020 Nov 25;63(22):13205-13227. doi: 10.1021/acs.jmedchem.0c00626. Epub 2020 Sep 11.

Corresponding Author: Jianxin Chen (Guangdong Provincial Key Laboratory of Veterinary Pharmaceutics Development and Safety Evaluation, South China Agricultural University; Guangzhou, China)

Abstract: The coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to more than 20 million people infected worldwide with an average mortality rate of 3.6%. This virus poses major challenges to public health, as it not only is highly contagious but also can be transmitted by asymptomatic infected individuals. COVID-19 is clinically difficult to manage due to a lack of specific antiviral drugs or vaccines. In this article, Chinese therapy strategies for treating COVID-19 patients, including current applications of traditional Chinese medicine (TCM), are comprehensively reviewed. Furthermore, 72 small molecules from natural products and TCM with reported antiviral activity against human coronaviruses (CoVs) are identified from published literature, and their potential applications in combating SARS-CoV-2 are discussed. Among these, the clinical efficacies of some accessible drugs such as remdesivir (RDV) and favipiravir (FPV) for COVID-19 are emphatically summarized. We hope this review provides a foundation for managing the worsening pandemic and developing antivirals against SARS-CoV-2.

2. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine

N Engl J Med. 2021 Feb 4;384(5):403-416. doi: 10.1056/NEJMoa2035389. Epub 2020 Dec 30.

Corresponding Author: Hana El Sahly (Departments of Molecular Virology and Microbiology and Medicine, Baylor College of Medicine; Houston, TX, USA)

Background: Vaccines are needed to prevent coronavirus disease 2019 (Covid-19) and to protect persons who are at high risk for complications. The mRNA-1273 vaccine is a lipid nanoparticle-encapsulated mRNA-based vaccine that encodes the prefusion stabilized full-length spike protein of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes Covid-19.

Methods: This phase 3 randomized, observer-blinded, placebo-controlled trial was conducted at 99 centers across the United States. Persons at high risk for SARS-CoV-2 infection or its complications were randomly assigned in a 1:1 ratio to receive two intramuscular injections of mRNA-1273 (100 µg) or placebo 28 days apart. The primary end point was prevention of Covid-19 illness with onset at least 14 days after the second injection in participants who had not previously been infected with SARS-CoV-2.

Results: The trial enrolled 30,420 volunteers who were randomly assigned in a 1:1 ratio to receive either vaccine or placebo (15,210 participants in each group). More than 96% of participants

received both injections, and 2.2% had evidence (serologic, virologic, or both) of SARS-CoV-2 infection at baseline. Symptomatic Covid-19 illness was confirmed in 185 participants in the placebo group (56.5 per 1000 person-years; 95% confidence interval [CI], 48.7 to 65.3) and in 11 participants in the mRNA-1273 group (3.3 per 1000 person-years; 95% CI, 1.7 to 6.0); vaccine efficacy was 94.1% (95% CI, 89.3 to 96.8%; P<0.001). Efficacy was similar across key secondary analyses, including assessment 14 days after the first dose, analyses that included participants who had evidence of SARS-CoV-2 infection at baseline, and analyses in participants 65 years of age or older. Severe Covid-19 occurred in 30 participants, with one fatality; all 30 were in the placebo group. Moderate, transient reactogenicity after vaccination occurred more frequently in the mRNA-1273 group. Serious adverse events were rare, and the incidence was similar in the two groups.

Conclusions: The mRNA-1273 vaccine showed 94.1% efficacy at preventing Covid-19 illness, including severe disease. Aside from transient local and systemic reactions, no safety concerns were identified. (Funded by the Biomedical Advanced Research and Development Authority and the National Institute of Allergy and Infectious Diseases; COVE ClinicalTrials.gov number, NCT04470427.).

3. Reports of Anaphylaxis After Receipt of mRNA COVID-19 Vaccines in the US—December 14, 2020-January 18, 2021

JAMA. 2021;325(11):1101-1102. doi:10.1001/jama.2021.1967

Corresponding Author: Tom Shimabukuro (Immunization Safety Office, Centers for Disease Control and Prevention; Atlanta, GA, USA)

In December 2020, the US Food and Drug Administration (FDA) issued Emergency Use Authorizations for 2 mRNA-based vaccines for prevention of coronavirus disease 2019 (COVID-19): Pfizer-BioNTech COVID-19 vaccine (EUA issued December 11; 2 doses, 3 weeks apart) and Moderna COVID-19 vaccine (EUA issued December 18; 2 doses, 1 month apart). Shortly after each authorization, the Advisory Committee on Immunization Practices issued interim recommendations for use.

Following implementation of vaccination, cases of anaphylaxis after administration of the Pfizer-BioNTech and Moderna vaccines began to be reported. Anaphylaxis is a life-threatening allergic reaction that can occur after vaccination, with onset typically within minutes to hours. The initial estimated reporting rates for anaphylaxis in the US were 11.1 cases per million doses administered of the Pfizer-BioNTech vaccine (December 14-23, 2020) and 2.5 cases per million doses administered of the Moderna vaccine (December 21, 2020-January 10, 2021). Since these early estimates were generated, millions more doses of both vaccines have been administered and safety monitoring has detected additional cases of anaphylaxis. This analysis updates the reporting rates of anaphylaxis in individuals following receipt of either the Pfizer-BioNTech or Moderna vaccine.

The Vaccine Adverse Event Reporting System (VAERS), the national passive surveillance (spontaneous reporting) system for adverse events after immunization,6 captured notifications and reports of suspected anaphylaxis following vaccination. Physicians at the Centers for Disease Control and Prevention (CDC) evaluated these reports and applied the Brighton Collaboration case definition for anaphylaxis to classify cases.

During December 14, 2020 through January 18,

2021, a total of 9 943 247 doses of the Pfizer-BioNTech vaccine and 7 581 429 doses of the Moderna vaccine were reported administered in the US (CDC unpublished data, February 2021). CDC identified 66 case reports received by VAERS that met Brighton Collaboration case definition criteria for anaphylaxis (levels 1, 2 or 3): 47 following Pfizer-BioNTech vaccine, for a reporting rate of 4.7 cases/million doses administered, and 19 following Moderna vaccine, for a reporting rate of 2.5 cases/million doses administered. Cases occurred after receipt of doses from multiple vaccine lots. Characteristics of reported cases of anaphylaxis following these vaccines are described in the Table.

CDC physician reviewers concluded that the clinical characteristics of anaphylaxis cases following both vaccines were similar. Furthermore, there were no apparent clinical differences between anaphylaxis cases with symptom onset within 30 minutes and those with symptom onset after 30 minutes (a 15-minute post vaccination observation period is recommended for all persons and a 30-minute period is recommended for those with a history of certain allergic reactions). Common signs and symptoms in anaphylaxis cases were generalized urticaria, diffuse erythematous rash, angioedema, respiratory and airway obstruction symptoms, and nausea. Twenty-one (32%) of the 66 case reports noted a prior episode of anaphylaxis from other exposures; prior exposures included vaccines (rabies, influenza A[H1N1], seasonal influenza, unspecified), contrast media (gadolinium-based, iodine-based, unspecified intravenous), unspecified infusions, sulfa drugs, penicillin, prochlorperazine, latex, walnuts, unspecified tree nuts, jellyfish stings, and unspecified exposures.

In 61 (92%) of the anaphylaxis cases, patients received epinephrine as part of emergency treatment. All 66 persons were treated in health care settings; 34 (52%) were treated in an emergency department and 32 (48%) were hospitalized (including 18 in intensive care, 7 of whom required endotracheal intubation). As determined by medical record review and follow-up with treating health care facilities and clinicians, of the 7 patients who required endotracheal intubation, median time to symptom onset was 6 minutes (range, <1-45 minutes), with all but one patient having onset within 11 minutes. All 7 of those intubated received epinephrine, 6 received corticosteroids, and 5 received antihistamines; facial, tongue, or laryngeal angioedema was present in 4 of these patients; and hospitalization ranged from 1 to 3 days. Sixty-one individuals (92%) with follow-up information available are known to have been discharged from care or had recovered at the time of report to VAERS. No deaths from anaphylaxis after vaccination with either product were reported.

Continued safety monitoring of mRNA COVID-19 vaccines in the US has confirmed that anaphylaxis following vaccination is a rare event, with rates of 4.7 cases/million Pfizer-BioNTech vaccine doses administered and 2.5 cases/million Moderna vaccine doses administered, based on information through January 18, 2021. When considered in the context of morbidity and mortality from COVID-19, the benefits of vaccination far outweigh the risk of anaphylaxis, which is treatable. Because of the acute, life-threatening nature of anaphylaxis, immediate epinephrine administration is indicated for all cases. CDC guidance on use of mRNA COVID-19 vaccines and management of anaphylaxis is available. All facilities administering COVID-19 vaccines should have the necessary supplies and trained medical personnel available to manage anaphylaxis.

4. Assessing the Safety of COVID-19 Vaccines: A Primer

Drug Saf. 2020 Sep 30: 1-6. doi: 10.1007/s40264-020-01002-6

Corresponding Author: Helen Petousis-Harris
(University of Auckland; Auckland, New Zealand)

Abstract: Vaccines against COVID-19 are being developed at speeds not previously achieved. With this unprecedented effort comes challenges for post-marketing safety monitoring and challenges for vaccine safety communication. To deploy these new vaccines fast across diverse populations, it is vital that robust pharmacovigilance and active surveillance systems are in place. Not all countries have the capability or resources to undertake adequate surveillance and will rely on data from those who can. The tools exist to assess COVID-19 vaccines as they are deployed such as surveillance systems, administrative data and case definitions for adverse events of special interest. However, stitching these all together and using them effectively requires investment and collaboration. This paper provides a high-level overview of some of the facets of modern vaccine safety assessment and how they are, or can be, applied to COVID-19 vaccines.

5. Progress in microneedle array patch (MAP) for vaccine delivery

Hum Vaccin Immunother. 2021; 17(1): 316-327. doi: 10.1080/21645515.2020.1767997

Corresponding Author: Jung-Hwan Park
(Department of BioNano Technology, Gachon University; Seongnam, Republic of Korea)

Abstract: A microneedle array patch (MAP) has been developed as a new delivery system for vaccines. Preclinical and clinical trials with a vaccine MAP showed improved stability, safety, and immunological efficacy compared to conventional vaccine administration. Various vaccines can be delivered with a MAP. Currently, microneedle manufacturers can mass-produce pharmaceutical MAP and cosmetic MAP and this mass-production system can be adapted to produce a vaccine MAP. Clinical trials with a vaccine MAP have shown comparable efficacy with conventional administration, and discussions about regulations for a vaccine MAP are underway. However, there are concerns of reasonable cost, mass production, efficacy, and safety standards that meet FDA approval, as well as the need for feedback regarding the best method of administration. Currently, microneedles have been studied for the delivery of many kinds of vaccines, and preclinical and clinical studies of vaccine microneedles are in progress. For the foreseeable future, some vaccines will continue to be administered with syringes and needles while the use of a vaccine MAP continues to be improved because of the advantages of less pain, self-administration, improved stability, convenience, and safety.

Political Epidemiology

Ex-CDC Chief on Challenge of Serving Trump During Pandemic

"Like a hand grasping": Trump Appointees Describe the Crushing of the CDC

The Era of Vaccine Diplomacy is Here

New Brighton Website

The BC website is continuously updated with BC news and activities. It also has an archive of BC case definitions and publications. The new website is http://brightoncollaboration.us Comments on the new website to bc-coordinator@taskforce.org, and keep an eye out for new content and features on the website as we go forward!

VSQ READERS

The Winter VSQ was emailed to over 900 readers. An estimate from the returned reader survey shows 30% of readers are from the US followed by Canada and India. Occupations are varied from clinical research to statistics to fund raising. All readers are invited to submit comments and articles to the VSQ.

New Brighton Collaboration Publications

In the recently launched website, newly published Brighton Collaboration articles and tools will be posted in English and some in Chinese, Spanish, French, or Portugese.

A couple of notable recent publications are:

- Standardized Template for Collection of Key Information for Benefit-Risk Assessment of Protein Vaccines
- Sensorineural Hearing Loss (SNHL) as an Adverse Event Following Immunization (AEFI): Case Definition & Guidelines for Data Collection, Analysis, and Presentation of Immunization Safety Data
- How to ensure we can track and trace global use of COVID-19 vaccines?

Articles and Comments to the VSQ are welcomed and invited.

The VSQ is produced by volunteers. But, there are unavoidable expenses for office supplies, etc. If you would like to help financially with the VSQ, click here and accept our thanks.

We would like to have a series of groups report their work on vaccines, vaccine safety, etc.

What have you done? What are you doing? What would you like to do?

If you received this VSQ from a colleague and would like to be added to our mailing list, please complete this form: https://bit.ly/3nPq3tE