Vaccine Safety Quarterly (VSQ) | January 2021

Brighton Collaboration 2.0

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

Dear Brightonians,

I'm pleased to write to you on this momentous occasion as the first COVID-19 vaccines are approved for emergency use in several countries. This event represents the culmination of a remarkable (~300 day) vaccine developmental process made possible by multiple factors, ranging from longstanding investment in biology to investing in manufacturing in parallel (vs. sequential) to key trials. If all goes as planned, the eventual global deployment in the coming months and years will hopefully begin to turn the tide against a viral pandemic that has devastated and disrupted broad swaths of human life in many countries.

Fortuitously, in May 2019, the Coalition for Epidemic Preparedness Innovation (CEPI) partnered with the Brighton Collaboration to launch the Safety Platform for Emergency vACcines (SPEAC) Project – with the goal of harmonizing the safety assessment of the various CEPI vaccine candidates: Lassa Fever, Middle East Respiratory Syndrome (MERS), Nipah, and Disease X (a future unknown emerging pathogen). By the time COVID-19 emerged in Spring of 2020, the various SPEAC work projects were already in place and ready to focus on it.

On March 12-13, 2020, at the advice of Dr. Paul-Henri Lambert (U. of Geneva), Brighton Collaboration and CEPI organized an urgent (our first virtual) scientific consensus meeting to better understand and hopefully prevent potential Vaccine-Associated Enhanced Disease (VAED) during vaccine development against COVID-19. The published meeting recommendations and newly developed VAED case definitions are helping the vaccine community to manage this potential risk.

The SPEAC team, especially Drs. Barbara Law, Wan-Ting Huang, and Matt Dudley, began the challenging task of screening the ever exploding medical literature for priority COVID-19 Adverse Events of Special Interest (AESI). This list has since been adapted by several key stakeholders (WHO, CDC, FDA, EMA) for their pharmacovigilance. Dr. Flor Munoz has also led the formation of several working groups to develop the needed COVID 19 standard Brighton case definitions (up to 10 budgeted currently) at an unprecedented pace (~4-6 months each). In addition to VAED, Acute Respiratory Distress Syndrome (ARDS), Multisystem inflammatory syndrome in children/adults (MIS-C/A), Pericarditis/Myocarditis and Thrombosis/Thromboembolism will soon be completed and posted on the Brighton Collaboration website. New Working Groups will be launched soon for Anosmia/Ageusia, Subacute Thyroiditis, Pancreatitis, and Rhabdomyolysis.

Speaking of the website, due to hard work by Matt Dudley, Gabrielle Corrigan, Lisa Chung, and Barb Law, the original content from BC 1.0 has been adapted and updated to our new home at the Task Force for Global Health. The following new features are worth highlighting. Firstly, all past Brighton Collaboration publications and related tools are now all available for free access for 10 years (courtesy of Elsevier, publisher of Vaccine) in one location. A searchable spreadsheet allows the user to specify the Brighton project source [e.g., SPEAC, Global Alignment of Immunization Safety Assessment in Pregnancy (GAIA)], the publication types (e.g., Case definition, Safety Template), Categories [e.g., body system (neurologic, respiratory, etc.) for case definitions. For many case definitions/guidelines, links to supplemental materials to aid their

use/implementation are also provided. Secondly, a COVID-19 specific section has been organized to aid research in this key domain.

As highlighted by Sonali Kochhar in the last issue of the VSQ, The Brighton Collaboration's BRAVATO (Benefit-Risk Assessment of Vaccines by Technology), formerly the Viral Vector Vaccines Safety or V3SWG, Working Group has developed standard templates for benefit- risk assessment of vaccine technologies for the main COVID-19 platforms. The templates aim to increase the comparability and transparency of information, provide a checklist-like tool for managing potential complex risks, and increase scientific literacy and discussion among stakeholders of otherwise highly technical information. Over a 6 month period in 2020, BRAVATO developed the templates for nucleic acid vaccines, protein vaccines, inactivated viral vaccines, live viral vaccines, and viral vector vaccines. On May 28th, 2020, the World Health Organization (WHO) Global Advisory Committee on Vaccine Safety (GACVS) recommended "any review of the safety of new vaccines be based on the appropriate Brighton Collaboration standardized templates for benefit–risk assessment of vaccines (by technology platforms) which offers a structured approach to evaluating safety,when available and approved. GACVS advised that templates be pilot-tested in a number of scenarios and then adapted accordingly." As more COVID-19 vacines progress through human trials, we hope more developers will use these templates to communicate with the public.

Another exciting development in 2020 has been the successful implementation of a meta-Data Safety Monitoring Board (mDSMB) in SPEAC under the leadership of Steve Black and Corry Dekker. Senior vaccine trialists with safety experience were assigned by SPEAC as liaisons to the DSMB for each CEPI-funded clinical trial. They report back to the mDSMB on a monthly basis to discuss any new signals and findings for lessons learnt. The last few months with the temporary halt of several Phase 3 trials have been especially active for the mDSMB.

Finally, as the introduction of COVID-19 vaccines beyond trials into the general population becomes reality, Brighton Collaboration has been active in COVAX, the new facility to enhance equitable access. We formed a new Digital Innovations in Vaccine Safety (DIVaS) Working Group that is thinking creatively to help solve some of the challenges in Low and Middle-income Countries (LMIC) for affordable high quality pharmacovigilance.

We hope Brighton Collaboration's partnership with all our global colleagues in 2021 will be equally fruitful Best wishes for a safe and restful remainder of the holidays in the meantime.

Best regards,

Robert (Bob) T. Chen MD MA

Scientific Director
Brighton Collaboration

COVID-19

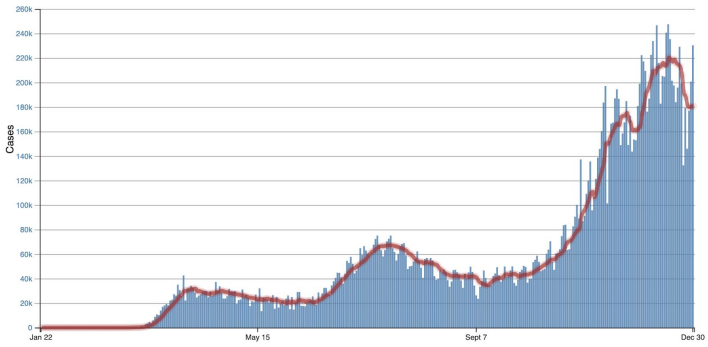
Over 82,000 citations coded COVID-19 are listed in PubMed. Many appear to be from China but from many other countries as well. The signs, symptoms, course, and sequelae of this disease are still evolving and probably will continue to do so for some time. This does not include any possible relevant entries in the preprint servers. One issue of the Journal of American Medical Association had 6 articles on COVID-19 and dermatology, cardiology, and etc. For the nonspecialist, Carlos del Rio has published another short summary. Johns Hopkins University maintains a COVID-19 dashboard which provides a daily global update for 30 countries.

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 "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. Initial information is that the current vaccines will give effective protection against this "UK" mutant as well. Autoantibodies have been in some cases and it has been proposed that they could account for some long term symptoms and Coagulopathy.

The New York Times continues to publish COVID-19 case counts as well as vaccine administration efforts in the US.



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

Treatment

Remdesivir has now been approved for use in certain cases; however, its effect appears to be modest. It is noteworthy that Francis Collins, the NIH director, convened a meeting quickly in April 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.

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 recently received emergency FDA approval. It is a unique double antibody drug which acts by attaching to COVID-19 virus particles and thereby reducing viral load. The Maryland health department has already sent a detailed instruction to members on the use of this drug. 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.

COVID-19 vaccine

The first successful vaccine trials have been completed. BioNTech-Pfizer (Pfizer, for short) and Moderna vaccines press releases claim about 95% success. A negative is that they require extreme cold for storage and transport. They both use a novel messenger RNA (mRNA) platform. A third vaccine, the so-called Oxford vaccine, has recently reported 70-90% success. This vaccine uses a viral vector platform and has advantages in stability and cost. However, there are some concerns about the conduct of the clinical trial. It was approved in the UK on December 28, 2020.

Since initial supplies of vaccine will be quite limited there are discussions concerning priority of distribution. Furthermore I have seen no discussion about world wide distribution. This is very relevant since the 3 vaccines mentioned were developed in 3 different countries, US. Germany and England. Apparently countries simply pre-ordered millions of doses last summer. About 200 possible vaccines are reportedly in some stage of development.

The London School of Public Health maintains a website with details of stage of development and vaccine type. But there is also a report that some trials are progressing slower than planned because of lack of supplies and patient recruitment. There has been much discussion about how a vaccine should be efficiently and fairly distributed. On December 1, 2020, 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.

Also in December 2020, the UK gave emergency approval to the BioNTech-Pfizer vaccine. The FDA approval process is more involved and detailed than that of the UK or EU. The FDA vaccine advisory committee met on December 2, 2020, and recommended approval of the Pfizer vaccine. Final approval was on December 11, 2020. The Moderna vaccine was approved one week later. More than one vaccine may be made available to more quickly satisfy global demand.

Some groundwork and planning for distribution have been done in anticipation of the availability of the vaccine. Allergic reactions are already reported in the press among the first recipients in the UK. Several individuals had a history of severe allergic reactions.

Thinking ahead 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-19but has been seen with SARS and MERS-Cov vaccines in animal models. At least six different platform technologies are being used in the attempt to develop this vaccine; many of which are new (See first article). A guideline for Coagulopathy will be available in 3-4 months

Some other thoughts on enhanced resistance to COVID 19 have resurfaced. One is that immunization against one virus may stimulate the immune enough to spill over to help protect against another virus. There is a 1960 russian study which says that polio

vaccine can protect against other viruses for one month.

Remarkably 9 potential COVId-19 vaccine manufacturers have signed a public pledge to maintain high standards to ensure that any vaccine they manufacture will be safe and efficacious.

There have been numerous articles in the press about people who say that they do not want to be among the first to get a vaccine when one becomes available. Apparently, this is because of a feeling that a vaccine may be rushed to market. Poor efficacy would be unfortunate because it could give individuals a false sense of confidence and undermine confidence in vaccines in general. But, 3 ex-presidents as well as the president-elect 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. There are also reports of individuals concocting their own "vaccines" and not only giving it to themselves but also to others. China and Russia have vaccines and both are reported to be exporting to other nations. Little is known about these products but see Literature reference #5 in this issue. 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.

Kudos to Brighton

Vaccine Industry Excellence (VIE) Award is organized at the World Vaccine Congress. This year's award, Brighton Collaboration was recognized as *Highly Commended* in this year's the Best Academic & Research Team Award. Congratulations to Brighton members and collaborators for all your hard work that made this group recognition possible!

VACCINE MISINFORMATION

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 "tipsheets" 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.

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 in Wikipedia. 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.

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 Vice-Chair Cathy Panozzo, Harvard and BC member Nadja Vielot, U of No Carolina.

The next journal club will be held **January 6, 2021 at 9:00am EDT**. We will discuss "Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia" by Logunov et al.

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

History

Edward Jenner and the Dairymaid
(from Hektoen International)

Smallpox has plagued mankind since time immemorial, causing huge epidemics with great loss of life and often changing the course of history. The disease could be prevented or ameliorated by variolation, the subcutaneous inoculation with fluid from smallpox lesions into non-immune individuals. Variolation had been used for centuries, even for members of royal families. It usually caused a milder disease than smallpox but had a 2-3 percent mortality rate.

The landscape of smallpox prevention changed dramatically in 1796 when an English physician, Edward Jenner, learned that persons would be immune to smallpox if they had had cowpox—a condition manifested by pustules on the udders of cows and sometimes causing a mild disease in humans. Cowpox is caused by the vaccinia virus (vacca = cow), a member of the pox family of orthopoxviruses, immunologically related to the variola virus of smallpox.

Hearing that persons exposed to cowpox were immune to smallpox, Jenner embarked on an experiment that today might have problems with an institutional review committee. In May 1796, he used material from the cowpox lesions of young dairymaid Sarah Nelms to inoculate the eight-year-old James Phipps. The boy had a mild fever for one day but no other symptoms. When two months later Jenner inoculated the boy with material from a fresh smallpox lesion, the boy did not develop the disease. At first the medical profession was skeptical of Jenner's finding, but eventually they were convinced. Within a few years doctors began to use vaccination; variolation was abandoned and became illegal (in England in 1840).

But from where did Jenner learn about cowpox? It had long been assumed it was from a milkmaid. Now it turns out that the milkmaid story is apocryphal, invented by Jenner's biographer several years after his death. It was John Fewster, a Gloucestershire surgeon, who made the first observation, noting that farmers who had had cowpox were immune to smallpox and could not be variolated against it. Fewster paid little attention to this fact but mentioned it at a meeting of the local medical society of which Jenner was a member. So it was from Fewster's observation that Jenner heard about the cowpox. It does not detract from Jenner's merit but debunks the "myth of the milkmaid.

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. An mRNA Vaccine against SARS-CoV-2 - Preliminary Report: *Report on the "Moderna Vaccine"*

N Engl J Med. 2020; 383:1920-1931. doi: 10.1056/NEJMoa2022483

Corresponding Author: Lisa A. Jackson (Kaiser Permanente Washington Health Research Institute; Seattle, WA, USA)

Background: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in late 2019 and spread globally, prompting an international effort to accelerate development of a vaccine. The candidate vaccine mRNA-1273 encodes the stabilized perfusion SARS-CoV-2 spike protein.

Results: After the first vaccination, antibody responses were higher with higher dose (day 29 enzyme-linked immunosorbent assay anti–S-2P antibody geometric mean titer [GMT], 40,227 in the 25-µg group, 109,209 in the 100-µg group, and 213,526 in the 250-µg group). After the second vaccination, the titers increased (day 57 GMT, 299,751, 782,719, and 1,192,154, respectively). After the second vaccination, serum neutralizing activity was detected by two methods in all participants evaluated, with values generally similar to those in the upper half of the distribution of a panel of control convalescent serum specimens. Solicited adverse events that occurred in more than half the participants included fatigue, chills, headache, myalgia, and pain at the injection site. Systemic adverse events were more common after the second vaccination, particularly with the highest dose, and three participants (21%) in the 250-µg dose group reported one or more severe adverse events.

Conclusions: The mRNA-1273 vaccine induced anti–SARS-CoV-2 immune responses in all participants, and no trial-limiting safety concerns were identified. These findings support further

development of this vaccine. (Funded by the NIAID and others; mRNA-1273 CT# NCT04283461).

2. Results of a randomized, double-blind phase II clinical trial of NY-ESO-1 vaccine with ISCOMATRIX adjuvant versus ISCOMATRIX alone in participants with high-risk resected melanoma.
Use of a new adjuvant, Iscomatrix.

J Immunother Cancer. 2020 Apr; 8(1):e000410. doi: 10.1136/jitc-2019-000410.

Corresponding Author: Jonathan S. Cebon (Cancer Immunology Programme, La Trobe University at Austin Health; Heidelberg, Victoria, Australia)

Background: To compare the clinical efficacy of New York Esophageal squamous cell carcinoma-1 (NY-ESO-1) vaccine with ISCOMATRIX adjuvant versus ISCOMATRIX alone in a randomized, double-blind phase II study in participants with fully resected melanoma at high risk of recurrence.

Results: The ITT population comprised 110 participants, with 56 randomized to NY-ESO-1/ISCOMATRIX and 54 to ISCOMATRIX alone. No significant toxicities were observed. There were no differences between the study arms in relapses at 18 months or for median time to relapse; 139 vs 176 days (p=0.296), or relapse rate, 27 (48.2%) vs 26 (48.1%) (HR 0.913; 95% CI 0.402 to 2.231), respectively. RFS and OS were similar between the study arms. Vaccine recipients developed strong positive antibody responses to NY-ESO-1 ($p \leq 0.0001$) and NY-ESO-1-specific CD4+ and CD8+ responses. Biopsies following relapse did not demonstrate differences in NY-ESO-1 expression between the study populations although an exploratory study demonstrated reduced (NY-ESO-1)+/Human Leukocyte Antigen (HLA) class I+ double-positive cells in biopsies from vaccine recipients performed on relapse in 19 participants.

Conclusions: The vaccine was well tolerated, however, despite inducing antigen-specific immunity, it did not affect survival endpoints. Immune escape through the downregulation of NY-ESO-1 and/or HLA class I molecules on tumor may have contributed to relapse.

3. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial: A report on the "Oxford Vaccine."

Lancet. 2020 Aug 15;396(10249):467-478. doi: 10.1016/S0140-6736(20)31604-4. Epub 2020 Jul20.

Corresponding Author: Andrew J. Pollard (Oxford Vaccine Group, University of Oxford; Oxford, UK)

Background: The pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) might be curtailed by vaccination. We assessed the safety, reactogenicity, and immunogenicity of a viral vectored coronavirus vaccine that expresses the spike protein of SARS-CoV-2.

Methods: We did a phase 1/2, single-blind, randomised controlled trial in five trial sites in the UK of a chimpanzee adenovirus-vectored vaccine (ChAdOx1 nCoV-19) expressing the SARS-CoV-2 spike protein compared with a meningococcal conjugate vaccine (MenACWY) as control. Healthy adults aged 18-55 years with no history of laboratory confirmed SARS-CoV-2 infection or of COVID-19-like symptoms were randomly assigned (1:1) to receive ChAdOx1 nCoV-19 at a dose of 5 × 1010 viral particles or MenACWY as a single intramuscular injection. A protocol amendment in two of the five sites allowed prophylactic paracetamol to be administered before vaccination. Ten participants assigned to a non-randomised,

unblinded ChAdOx1 nCoV-19 prime-boost group received a two-dose schedule, with the booster vaccine administered 28 days after the first dose. Humoral responses at baseline and following vaccination were assessed using a standardised total IgG ELISA against trimeric SARS-CoV-2 spike protein, a multiplexed immunoassay, three live SARS-CoV-2 neutralisation assays (a 50% plaque reduction neutralisation assay [PRNT50]; a microneutralization assay [MNA50, MNA80, and MNA90]; and Marburg VN), and a pseudovirus neutralisation assay. Cellular responses were assessed using an ex-vivo interferon- γ enzyme-linked immunospot assay. The co-primary outcomes are to assess efficacy, as measured by cases of symptomatic virologically confirmed COVID-19, and safety, as measured by the occurrence of serious adverse events. Analyses were done by group allocation in participants who received the vaccine. Safety was assessed over 28 days after vaccination. Here, we report the preliminary findings on safety, reactogenicity, and cellular and humoral immune responses. The study is ongoing, and was registered at ISRCTN, 15281137, and ClinicalTrials.gov, NCT04324606.

Findings: Between April 23 and May 21, 2020, 1077 participants were enrolled and assigned to receive either ChAdOx1 nCoV-19 (n=543) or MenACWY (n=534), ten of whom were enrolled in the non-randomised ChAdOx1 nCoV-19 prime-boost group. Local and systemic reactions were more common in the ChAdOx1 nCoV-19 group and many were reduced by use of prophylactic paracetamol, including pain, feeling feverish, chills, muscle ache, headache, and malaise (all p<0·05). There were no serious adverse events related to ChAdOx1 nCoV-19. In the ChAdOx1 nCoV-19 group, spike-specific T-cell responses peaked on day 14 (median 856 spot-forming cells per million peripheral blood mononuclear cells, IQR 493-1802; n=43). Anti-spike IgG responses rose by day 28 (median 157 ELISA units [EU], 96-317; n=127), and were boosted following a second dose (639 EU, 360-792; n=10). Neutralising antibody responses against SARS-CoV-2 were detected in 32 (91%) of 35 participants after a single dose when measured in MNA80 and in 35 (100%) participants when measured in PRNT50. After a booster dose, all participants had neutralising activity (nine of nine in MNA80 at day 42 and ten of ten in Marburg VN on day 56). Neutralising antibody responses correlated strongly with antibody levels measured by ELISA (R2=0·67 by Marburg VN; p<0·001).

Interpretation: ChAdOx1 nCoV-19 showed an acceptable safety profile, and homologous boosting increased antibody responses. These results, together with the induction of both humoral and cellular immune responses, support large-scale evaluation of this candidate vaccine in an ongoing phase 3 programme.

4. Influenza immunization and COVID-19. A timely, relevant discussion.

Vaccine. 2020 Sep; 38(39):66078-6079. doi: 10.1016/j.vaccine.2929.97.058. Epub 2020 Jul 29.

Corresponding Author: Helena C. Maltezou (National Public Health Organization; Athens, Greece)

Influenza and COVID-19 can present with similar symptoms, and co-infections with a more severe course, complications or a fatal outcome have been recorded. Beyond that, COVID-19 and seasonal influenza share the same high-risk groups and both can prove detrimental for older persons and persons with chronic co-morbidities, including obese persons and residents of long-term care facilities. Given the uncertainties of a second COVID-19 epidemic wave, and when a COVID-19 vaccine might be available, influenza immunization should be regarded as an integral component of

preparedness and response plans for the COVID-19 pandemic. Prioritizing influenza immunization of pregnant women, persons with co-morbidities, the elderly, and residents of long-term care facilities is absolutely justified. Increasing influenza vaccine uptake by health care providers is also imperative in order to protect the essential healthcare services from influenza-associated absenteeism and the vulnerable patients they care for.

5. Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomized phase 1/2 studies from Russia.
The only information I have seen on the Russian vaccine, Sputnik V.

Lancet. 2020 Sep 26;396(10255):887-897. doi: 10.1016/S0140-6736(20)31866-3. Epub 2020 Sep 4.

Corresponding Author: Denis Y. Logunov (Gamaleya National Research Centre for Epidemiology and Microbiology; Moscow, Russia)

Background: We developed a heterologous COVID-19 vaccine consisting of two components, a recombinant adenovirus type 26 (rAd26) vector and a recombinant adenovirus type 5 (rAd5) vector, both carrying the gene for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike glycoprotein (rAd26-S and rAd5-S). We aimed to assess the safety and immunogenicity of two formulations (frozen and lyophilised) of this vaccine.

Methods: We did two open, non-randomised phase 1/2 studies at two hospitals in Russia. We enrolled healthy adult volunteers (men and women) aged 18–60 years to both studies. In phase 1 of each study, we administered intramuscularly on day 0 either one dose of rAd26-S or one dose of rAd5-S and assessed the safety of the two components for 28 days. In phase 2 of the study, which began no earlier than 5 days after phase 1 vaccination, we administered intramuscularly a prime-boost vaccination, with rAd26-S given on day 0 and rAd5-S on day 21. Primary outcome measures were antigen-specific humoral immunity (SARS-CoV-2-specific antibodies measured by ELISA on days 0, 14, 21, 28, and 42) and safety (number of participants with adverse events monitored throughout the study). Secondary outcome measures were antigen-specific cellular immunity (T-cell responses and interferon-γ concentration) and change in neutralising antibodies (detected with a SARS-CoV-2 neutralisation assay). These trials are registered with ClinicalTrials.gov, NCT04436471, and NCT04437875.

Findings: Between June 18 and Aug 3, 2020, we enrolled 76 participants to the two studies (38 in each study). In each study, nine volunteers received rAd26-S in phase 1, nine received rAd5-S in phase 1, and 20 received rAd26-S and rAd5-S in phase 2. Both vaccine formulations were safe and well tolerated. The most common adverse events were pain at the injection site (44 [58%]), hyperthermia (38 [50%]), headache (32 [42%]), asthenia (21 [28%]), and muscle and joint pain (18 [24%]). Most adverse events were mild and no serious adverse events were detected. All participants produced antibodies to SARS-CoV-2 glycoprotein. At day 42, receptor binding domain-specific IgG titres were 14 703 with the frozen formulation and 11 143 with the lyophilised formulation, and neutralising antibodies were 49·25 with the frozen formulation and 45·95 with the lyophilised formulation, with a seroconversion rate of 100%. Cell-mediated responses were detected in all participants at day 28, with median cell proliferation of 2·5% CD4+ and 1·3% CD8+ with the frozen formulation, and a median cell proliferation of 1·3% CD4+ and 1·1% CD8+ with the lyophilised formulation.

Interpretation: The heterologous rAd26 and rAd5 vector-based COVID-19 vaccine has a good safety profile and induced strong humoral and cellular

immune responses in participants. Further investigation is needed of the effectiveness of this vaccine for prevention of COVID-19.

A Smallpox Warrior

"J. Michael Lane, a globe-trotting epidemiologist who waged a 13-year war against the scourge of smallpox and led the final drive for its global eradication in 1977, when the last known vestige of the disease was snuffled out in East Africa, died on Wednesday at his home in Atlanta. He was 84." (New York Times, Oct. 21, 2020)

Political Epidemiology

- Trump administration buries detailed CDC advice on reopening
- Trump aides undercut Fauci as he speaks up on virus concerns
- So it has come to this
- CDC testing guidance was published against scientists' objection
- Battered by Trump, Robert Redfield of the C.D.C. Faces ...
- White House Blocks New Coronavirus Vaccine Guidelines ...
- CDC Issues Increasingly Assertive Advice as Coronavirus
- Trump Appointees Describe the Crushing of the CDC

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!

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?

VSQ READERS

The Fall 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.

Articles and Comments to the VSQ are welcomed and invited.

Ode to 2020

Kevin A. Wilson

‘Twas some days before Christmas—how many I’m not sure
(The days ran together; everything was a blur).
All the houses were locked down from COVID-19,
With everyone wishing for the promised vaccine.
The children were nestled and sleeping just fine.
They were all tuckered out from their classes online.

And mamma in her kerchief and I in my cap
Had just sanitized our hands and hung up our masks.
The year had been hard. We were due a vacation.
But the thing wanted most? Emergency use authorization.

Then out on the lawn there arose such a clatter,
I assumed it was another 2020 disaster.
I ran to the window and put on my mask,
But what would I see? I was too scared to ask.

The neighbors were quiet and socially distant,
Awaiting the time they’d be COVID resistant.
But despite travel bans, there then did appear
A miniature sleigh and eight tiny reindeer.

But this wasn’t Santa. His gut wasn’t paunchy.
It was the trusted presence of Anthony Fauci.
More rapid than eagles, at warp speed they came,
And he whistled, and shouted, and called them by name:
“Now Pfizer! Now Sanofi! Now Johnson & Johnson!
“On Moderna! On BioNTech! On Adaptive and Amgen!
To the top of the porch! To the top of the wall!
Now vaccinate, vaccinate, vaccinate all!”

As a virus expelled by a cough or a sneeze
When it meets plexiglass rises up on the breeze;
So up to the house-top the pharma all flew,
With the sleigh full of hope, and Dr. Fauci, too.
And then, in a twinkling, I heard on the roof
The prancing and pawing of each little hoof.
As I drew in my head, and was turning around,
Down the chimney Fauci came with a bound.

He was dressed in a suit, as was always his way,
And his neatly cut hair was a smart silver-grey.
A chart in one hand, a syringe in the other,
And a medical bag—a gift from his mother.

The wisdom in his eyes and the knowledge in his head
Soon gave me to know I had nothing to dread.
With his reassuring smile covered up with a mask,
His no-nonsense style led him straight to the task.
He sprung to my side as I rolled up my sleeve,
And he stuck in the vaccine as quick as you please.
He flew to the bedroom, gave mamma a shot,
Then vaxxed both our kids without waking them up.

Inoculations complete, he returned to the chimney,
And gave me a pamphlet about what he put in me.
Then raising his finger but not touching his nose,
And giving a nod, up the chimney he rose.
“C’mon, team!” he said. “We’ve a great opportunity.
If we vaccinate more we can reach herd immunity!”
Then he yelled back to me, as the sleigh quickly rose,
"I’ll be back in a fortnight for the follow-up dose."

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