Vaccines and Immunology of COVID-19 Questions and Answers

Thank you everyone for submitting questions. We have answered the questions to the best of our ability. Please remember that we bring in the experts to give you expert advice but the views presented are our views and the views of our guests, and not the views or policies of the University of Notre Dame. The information provided is not intended to serve as, nor should be interpreted as, specific medical advice or a substitute for the advice of an individual's personal health practitioner.

Questions and Answers

Please clarify what "peer-review" actually is

Scientific peer review happens when a group of scientists complete a study and submits a manuscript for publication describing the results or when they submit a grant proposal for funding. The journal's editors send the article to other scientists that work in the same area and those reviewers provide feedback and recommend if the study is sound and worthy of publication. The authors have an opportunity to revise their manuscript and conduct additional experiments. Only articles that meed good scientific standards are accepted for publication. Grant proposals (at least for the National Institute of Health and the National Science Foundation) are similarly reviewed.

One of the tragedies of this pandemic has been the reliance on 'pre-reviewed' publications that gain immediate press traction before undergoing peer review. This is a double edged sword. (See the HCQ disaster, for example.)

Definitely pre-release, non-peer-previewed publications has the potential for misinformation to be spread. That being said, even peer-reviewed work can be misinterpreted by non-scientists and scientists alike. This is why science literacy is so important…don't believe scientists, believe the science! The hydroxychloroquine disaster had multiple levels of misinformation. Not only were their pre-publications that were misinterpreted, there were published, peer-reviewed manuscripts that had to be retracted because scientists (that didn't review the original submission) highlighted inconsistencies. So, while the scientific review process didn't work initially it did work in the end. In addition, to the misinterpretation of the data misinformation was spread by politicians. The use of hydroxycholoroquine is now NOT recommended because it can cause harm to COVID-19 patients.

"Immunity" or perhaps more precisely, an immune response can be a source of problems, if i remember correctly the meningitis pathology can be caused by the immune system attacking the meninges, not the bacteria itself. Can this mechanism be a cause of COV.

Certainly much of the pathology associated with SARS-CoV-2 infection is thought to be immune mediated. For many severe cases the 2nd phase of the disease and in many that are hospitalized the pathology is thought to be due to thrombosis (clotting) and tissue damage associated with uncontrolled inflammation. There are likely different types of pathology associated with different underlying conditions and different patients and we are still relatively early in the pandemic and continue to learn more and more about the disease.

"Reinfection" definition will depend on the performance characteristics of the diagnostic tests that have been used to call the person 'cured' in the first place.

Thank you for the comment. Yes there is a possibility that someone could be defined as having a re-infection if they received a false positive diagnostic test in the first place, or if they received a false negative test upon 'cure' of the first infection. The only way to be truly sure of reinfection is if the virus from the first infection and the second infection is genotyped (sequenced) to ensure that they are different infections. At the moment, there have only been 4 reports of true infection, 2 that had milder disease (Netherlands/Belgium and Hong Kong) and 2 that had more severe disease. (Nevada, US and Ecuador) the 2nd time.

My daughter is a ND student, I check the HERE dashboard daily and the COVID program, testing, surveillance, etc seems to be working well (low positives/ high testing). This seems to be a natural population that could provide insights on reinfection rate.

This is an interesting idea but it is likely the rate of transmission that is occurring on campus and the small sample size will not be enough to say anything definitively. Given that there have been only 4 cases in the world officially documented, it is unlikely that we have enough infection on campus to effectively assess this question.

Will people with certain autoimmune diseases be eligible for a live vaccine for COVID-19?

Certainly individuals with primary immunodeficiencies many not be eligible for a live vaccine because they can't mount an effective immune response. The live vaccines are vaccines using a vector virus (a virus that doesn't cause disease in humans or a virus that causes mild symptoms, like the common cold) that have been genetically engineered to express part of the SARS CoV-2 virus (usually the SPIKE protein). For more information about the types of vaccines check out the informational tutorial or the New York Times Vaccine Tracker. In terms of autoimmune disorders, it is usually not the autoimmune disease that the patients have to be worried about but rather the immunsuppressive drugs that they might be taking to control their autoimmune disease that could weaken there immune response to the live virus.

Do you answer the questions submitted prior on the google doc in this forum.

Thank you for posing this question because it stimulated us to go through and answer the questions. We apologize for the delay in getting the answers posted, but hope they are helpful nonetheless.

How long does immunity from the vaccine last? I am guessing it is better to get higher neutralizing antibodies to the vaccine? What about Cytotoxic T Cells? So which vaccine should I use (which one will give me the highest antibodies)? What about 3 doses?

We don't know how long the immunity from the different vaccines will last. Some vaccines only last a short time (e.g. influenza virus), others an intermediate time (e.g. tetanus toxoid vaccine/~10 years) and others assumed to be life-long (e.g. measles). So, the jury is out as to how long immunity will last to the various vaccine formulations. There are a variety of factors that go into whether or not immunity induced by vaccines lead to long-term immunity or not (formulation, dose, adjuvants, route of inoculation, boosting, type of vaccine, etc.). We will just have to wait and see what the current COVID-19 vaccines induce in terms of immunity. That is one reason why it is important to have the vaccine trials last for 2-3 years.

One reason that we get a yearly flu vaccine is because of the different strains that we are exposed to year to year so the vaccine we receive one year might not provide effective immunity to the virus that is circulating in the population the following year. The other reason is that antibodies wane with time and for optimal protection it is recommended that we receive a vaccine every year. There are a variety of flu vaccines to choose from but the most common is a quadrivalent (against 4 flu strains) that is grown in eggs. There is also an egg free variety of this vaccine. One hypothesis is that the quadivalent vaccines do not induce long lasting antibodies because these vaccines lack an adjuvant (a substance that enhances immune responses). There is also the FluMist vaccine that is a live attenuated vaccine (4 flu strains) and a trivalent vaccine with adjuvant that is recommended for those 65 and older.

Mary Ann and Heidi, Thank you!

Thank you for listening!!

The Oxford/Astra Zeneca vaccine has had two SAE's, the second being transverse myelitis that is extremely worrisome. The first one was supposedly an 'unmasking' of previously undiagnosed Multiple Sclerosis. Uncertainty of a causal relationship has led t

It is not uncommon in large scale vaccine trials for some participants to become ill and the trials paused so that safety can be evaluated. That is why it is so important not to rush these trials and follow strict procedures. The FDA and international regulators reviewed all of the data and deemed that the trial was safe to resume. The Astra Zeneca trial is now up and running in all of the original countries.

Will only one vaccine be approved or will we need to choose between several?

It is possible that we will be able to choose between several. One risk is that if a vaccine gets an EUA early, perhaps not the most effective, and the other studies decided it is not worth it to continue development of their vaccine. In addition, if an EUA is granted in the middle of a trial, all the individuals in the placebo (unvaccinated) group have to be offered the vaccine. If many of them choose to be vaccinated then there might not be enough individuals in the 'control' arm of the study to statistically determine if there are significantly more adverse effects.

Is there a phase IV clinical trial segment in vaccine development that would typically study safety (eg. rare side effects) and efficacy in large/mass more heterogeneous populations?

The Pfizer group expanded its study group from 30,000 to 43,000 individuals specifically to include more heterogeneous populations. These trials are officially set to end in 2022 to try and determine if there are any long term safety problems. Phase 4 clinical trials, sometimes called post-marketing surveillance trials, are designed to identify long term side effects. Some side-effects, like Guillian-Barre syndrome, and inflammatory disorder of the peripheral nerves outside of the brain and spinal cord than can result in partial paralysis for a while (most people recover), is rare (1 in 100,000 vaccinations) so large scale vaccination would have to occur before this side effect would be evident.

Are people being exposed to the virus in these trials?

For all of the current trials exposure will be through natural transmission in the community. Recently a human challenge trial was announced to begin in January in the UK. Young, healthy people will be intentionally exposed to the virus.

How do we avoid another rotavirus disaster..taken off market due to side effects.

All we can say is SAFETY! SAFETY! SAFETY! And do not rush the science.

Thank you so much for this series. As a retired Medical Technologist/CLS, I'm finding it a great refresher with sive federal response to this pandemic. My husband is in remission from cancer and I worry about him every day. We have curtailed our activities and are extremely careful about wearing a mask, social distancing, and good infection control practices. My question for next week is about our public health failure to contain this pandemic. What could and should we have done differently to control the transmission and ensure that the infection didn't run rampant? some interesting new information. My main focus in my career was Microbiology but I had a strong interest in Immunology as well (because they are so connected). I find myself utterly dismayed by the lack of a coherent and comprehend

We think that constant reliable information from our leadership would have helped. In addition, the dismantling of the Federal Pandemic Response Unit was not helpful either. It is unfortunate that public health has become so politicized in this country and that political appointees with limited or no public health experience are involved in the messages coming from our most trusted health institution, the Centers for Disease Control.

Thank you for your Oct. 12th webinar. It was very informative and helpful.

Thank you for participating!

How do the vaccines differ?

Please refer to the informational tutorial or check out the New York Times Vaccine Tracker.

You've wasted my time with dysfunctional webinar technology - disgusting!!

We are so sorry that you had trouble with the webinar technology and that we have wasted your time. Hopefully you were able to view the session at a later date. Please email us at consider@nd.edu so that we can make sure that you can sign on in the future.

How can one confirm the status of the COVID-19 epidemic in a region? For example, it seems as if Saint Joseph county has a recent rise in infections, but the state website statistics don't seem to bear that out.

There are several ways to monitor and track COVID cases in a particular county or state.

(a) For St. Joseph County, the best way is to track data through the regular press releases found here: https://www.sjcindiana.com/1855/Press-Releases.
(b) For the State of Indiana, a dashboard has been created to track data by county. It can be found here: https://www.coronavirus.in.gov/2393.htm
(c) For US States and Counties, Johns Hopkins University offers an interactive map that tracks cases throughout the US. It is found here: https://coronavirus.jhu.edu/us-map

Additionally, we have a weekly tutorial on our webpage on tracking COVID-19 in St. Joseph County. The goal with the tutorial is to help improve public health literacy as it relates to COVID-19.

Finally, you are correct in saying that the county data does not always align with the state data. There are a few factors that contribute to this issue. First, there may be a delay in reporting in testing and second, not all negative tests may be reported to the State (during the first several months of the pandemic this was a significant factor).

It seems that everyone is assuming that we will have a vaccine. How confident are you that any of the 30+ (might be more by now) vaccine trials will be successful?

It is likely that we will have an effective vaccine at some point. The timing is difficult to predict. The fastest vaccine to be developed was the Mumps vaccine in 1967 and that took four years! However, given the severity of the pandemic, there is a concentrated effort to develop a vaccine(s) much more quickly.

Here are two sites where you can track the vaccine trials in great detail: https://www.raps.org/news-and-articles/news-articles/2020/3/covid-19-vaccine-tracker

and https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.htm

How does one measure the relative effectiveness of different types of vaccines and would one be more likely to be protected by taking a combination of the different types?

That is a complicated question because it would depend on what vaccines you are talking about. The majority of the vaccines are targeting the SPIKE protein so on first thought it would seem redundant to be immunized with two that target the SPIKE protein, however, it may be that their different formulations could change the response. Of course if one generates enough neutralizing antibodies then another vaccine would just be redundant. If a different vaccine generates cytotoxic T-cells then it might generate a longer, different type of immunity. So, it is complicated to answer this question and will depend on what vaccines are available.

My question is how long will protection last? Essentially, is there (or do you think there will be) a serological immune marker of protection or will we have to wait for breakthrough cases? And if neutralizing antibodies are felt to be the mechanism of protection, shouldn't I receive the vaccine that elicits the highest antibody response? Or perhaps get 3 doses instead of 2 to maximize my response?

See answers above for how long the protection will last. There is some evidence with the coronaviruses that cause the common cold do not cause a long term immunity. Vaccines, however, can sometimes cause a different type of immunity than natural infection. Usually, natural infection will induce better immunity but not always. Each vaccine has been formulated with the number of boosts that induces optimal neutralizing antibodies so extra doses will likely not be better.

Comment: The emergence of beta-coronaviruses that cause SARS in 2002, MERS in 2011, and now COVID-19 indicate that we should address not only COVID-19, but also prepare for the re-emergence of SARS and MERS, and possible future emergence of currently undiscovered beta-coronaviruses. Basic research has begun to identify epitopes that are highly conserved among human and animal coronaviruses that could be the basis for a pan-coronavirus vaccine. Here is a link to a preprint (not yet peer-reviewed) https://pubmed.ncbi.nlm.nih.gov/33024971/

Great comment and you are correct, it is a good idea for us to try and develop tools to combat the next, unknown, pandemic!

I heard about a receptor in the lungs researchers were looking at to determine if some people were more susceptible to COVID-19 because of their genetics. Is that receptor the Ace2 receptor?

There has been a study assessing ACE2 genetic variants in an Italian population and they found that there were more variants in the control population than those infected with SARS CoV-2. This study suggested that this might mean that certain ACE2 variants were more likely to result in SARS CoV-2 infection but this was not assessed.

What is adaptive about the ADE process? Are the receptors on the cytotoxic t-cells so they let the virus in and then kill it?

Antibody Dependent Enhancement (ADE) is when antibodies, is when antibodies bind the virus and mediate cell infection through a receptor on some cells that recognize the antibody and thus enhances infection rather than neutralizes infection. This general mechanism is useful for eliminating some types of pathogens that cannot escape the vacuole inside of the cell like SARS CoV-2 can (see tutorial from the first session). So it is adaptive because it uses antibodies and can be a mechanism to eliminate some invading microorganisms, but just not SARS CoV-2.

The receptors on the surface of cytotoxic T-cells recognize small parts of the virus that are presented to human self proteins. The cytotoxic T-cell then kills the infected cell, the virus can't replicate without a living cell.

When you donate blood and get an antibody test, the presence of which antibodies is being tested?

Usually antibody tests are testing for IgG and maybe IgM antibodies specific for SARS CoV-2. It depends on the test being run and we are not sure what tests the RedCross is using specifically.