Dr. Delgado COVID-19 Update 4-08-20

Risk of reinfection?

There remains some level of uncertainty as to this question. Some reports have circulated that some patients seemed to have recovered, but then tested positive again. A recent report involving 51 patients from Korea's Center for Disease Control & Prevention stated the virus was likely just reactivated, rather than patients becoming reinfected. A virus may lay dormant at undetectable levels in human cells after an infection such as in HIV. For reasons that are unclear, some viral particles can reactivate within the body, but as to whether this may lead to additional viral spread is considered unlikely.

This hypothesis could explain why some patients could produce an additional positive test. In addition, the rate of false positives is such that a second test showing another positive result could be erroneous in up to 20% of cases. Lastly, patients with secondary positives may have just been prematurely cleared of their primary infection and were still infected when retested.

Retrospectively, many studies assessing immunity in previous coronaviruses strains, such as the common cold, show that immunity is generally conferred with an infection and statistically can last for 1-2 years. This is consistent and reproducible.

How robust an immune response is quantitatively and when that response peaks and then eventually wanes is the key as to the risk of re-infection in regards to this particular coronavirus strain.

Will it mimic previous coronaviruses? Likely, but too early to know definitively.

More to follow on this topic as we move forward.

Mutation

Viruses evolve by mutating. That is, there are changes in their genetic code over time that allows a virus to survive by enhancing its capacity to infect and spread. How fast this occurs and knowing where these mutations are occurring within the viral genome constitute a key point of emphasis in developing a vaccine to combat any virus. What we are finding is that the Covid-19 virus appears to be mutating more slowly than the seasonal flu which may allow scientists to develop a vaccine much more efficacious than for the flu.

DNA sequencing of a virus has improved exponentially over time. Using powerful computers, scientists can generate models to not only replicate the viral genome, but predict their most likely course of mutations. Knowing which gene sequences are likely mutating could be the key in either drug or vaccine design. This technology may generate strategies to directly combat the actual mechanisms within pathogens that allow them to proliferate.

One such initiative is Nexstrain, an open-source project that provides users real-time reports of the spread. Most recently, they have been spearheading the evolutionary tracking of COVID-19 by providing a real-time analysis, as well a situational report to be readable by the general public.

Based on the current data available, it seems as though the seasonal flu mutates roughly four times as fast as Covid-19. The fact that the seasonal flu mutates so quickly is precisely why it is able evade more accuracy as to its yearly vaccine design. Therefore, the significantly slower mutation rate of Covid-19 gives us hope for the potential development of a more effective and long-lasting vaccine against this virus.

Vaccine update

The most impactful exit strategy to this pandemic is the production of an effective vaccine.

Multiple companies are racing to produce potential vaccines and investing billions of dollars into their development and production. This is due to the global nature of this pandemic and it poses many logistical and financial questions that need to be addressed.

The endeavor to produce a vaccine for this pandemic means that an acceleration of this process will need to be on a scale that is unprecedented. The scale in regards to production will need to be geared toward immunizing 6-7 billion people over a compressed period of 2-3 years. This will require a level global coordination and cooperation that must rise above any current bureaucratic and financial barriers that currently exist.

Advocacy, both private and public, for the allocation of funds to guarantee substantial purchase commitments from multiple manufacturers of vaccines is garnering momentum. This guarantee would create a clear incentive to ramp up manufacturing capacity and production of potential vaccine candidates.The most promising vaccine platforms would need to

be chosen and, regardless of their end result, would be urged to proceed in hopes that one, if not more, could succeed in finding an effective vaccine.

In addition, financial assurances might entice manufacturers to share their platforms in partnerships with other manufacturers globally in real time which would be for the greater good globally. I don't see any other sensible alternatives based on the data and current risk. Public policy, with a global perspective, may need to quickly accept this reality and move forward in a cohesive fashion.

Lastly, if successfully created, the allocation of any vaccine fairly will be a monumental undertaking. Countries cannot protect themselves or their interests by only vaccinating their populations when the problem is global in nature. Leaving it up to market mechanisms is not an approach that would likely yield a judicious distribution. Supplies will be very limited initially and a dialogue needs to ensue now as to prioritization of any future allocations.

As to promising vaccine candidates? It still remains too early to glean if any one is more promising than the next at this time. There are numerous candidates and some are have already entered pre-clinical and clinical trials. I will continue to monitor this topic accordingly.

Treatments

Results from Gilead Sciences and their clinical trials in China are expected this month.Their product, Remdesivir, is one of the potential Covid-19 treatments that appears furthest along in the development process. Hopefully, the results will answer two key

questions: Is it effective? And under which circumstances or clinical scenarios?

Remdesivir works against an array of viruses, including other coronaviruses, in labs so clinical trials were instituted at the onset of the outbreak in humans. Two trials, one for patients with severe Covid-19 infections and the other for those classified mild to moderate will be reported. The end point will focus on how much improvement in symptoms is noted in either case against placebo.

Even if the results show no clear benefits overall, it may still yield information as to the impact it may have if given earlier in the course of their illness. This would be similar in nature to current anti-viral drugs available for the flu.

End of life

A lot of discussion in the medical community as to end of life decisions during this pandemic has circulated in medical publications. I have been averse to broaching this topic by email to this point, but feel I can no longer delay this essential dialogue.

This conversation ideally entails a personal dialogue between the physician and patient. It is best to be done in advance of any potential need and after the patient has pondered what their choices likely will be. Usually, this occurs after an individual has an honest dialogue with any partners, family or friends as to their clear wishes. Subsequently, they share their thoughts with their physician and the appropriate legal forms are executed to reflect those choices.

This pandemic has made the need for this dialogue critical for all adults, but especially for those who would most likely need intensive medical intervention. In the new reality of Covid-19, invasive treatments (i.e. mechanical ventilation) may lead to more distress and physical separation from family and friends, often without changing the course of the illness.

If all adults, especially those older and with chronic medical issues, clearly express their priorities for care during a serious illness, we could better align patients' care with the personal values and priorities and those of society.

Serologic Tests and Office Update

I hope to provide updates on both of these fronts in my next report scheduled for Friday, April 10.

Continue to persevere and focus on that you can control.

R. Delgado, MD & staff