

# Dr. Delgado COVID-19 Update 6-22-20

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## More on Immunity

We still have a lot of questions that remain unanswered as to how Covid-19 immunity works. As we work our way towards a possible vaccine and continue to pin our hopes on possible herd immunity, we need to delve further into what immunity might mean.

For the general public, immunity means protection from a disease. For many immune specialists “immune” and “not immune” are more a gradient than a binary. Immunity is not always absolute and any immune response has many potential endpoints.

Immunity mostly refers to the production of antibodies by our body’s immune system. This can be a bit misleading. A study preprint from England earlier this month actually measured the antibody levels in patients who were positive for COVID-19 and found that between 2 to 8.5% didn’t even develop detectable antibodies. The presumption is that this group (typically younger patients)

likely fought off the virus through cell-mediated arms of the immune system — white blood cells and cytokines that directly engage and kill pathogens — rather than antibodies to neutralize the virus.

Infections that cause severe symptoms are more likely to lead to a stronger immune response which would also help encourage a stronger and longer lasting immunity thereafter.

On the flip side, a milder asymptomatic case is likely to yield lower antibody levels. A recent study published in Nature magazine points out that asymptomatic patients did appear to develop a lower yield of antibody levels. This does not necessarily imply that their immune system is less likely to fight off infection and it's just too early to make any definitive conclusions.

Other research has demonstrated that those who mount a significant inflammatory reaction might be producing a potentially more detectable and robust immune response. Growing evidence may underscore the importance of a cell-mediated immune response for fighting coronavirus infection in conjunction with an antibody response.

What this means for any potential vaccine remains the question. We still don't know what kind of immunity —

temporary, permanent, absolute, relative (only minimizes symptoms), etc., — we will attain. It won't be until phase III trials (which directly measure the vaccine's efficacy) that we'll have a clearer picture as to the relationships between antibody level, the role of cellular immunity and what kind of a response a vaccine will need to elicit to provide true protection.

## **Prompt Response**

Three factors enable a meaningful comparison with other industrialized nations as to whether or not more cohesive and aggressive measures taken at the onset of the pandemic may have led to a lower death toll.

One, in each of these countries used in the comparison - Australia, Germany, Singapore and South Korea - roughly 80% or more of the population lives in urbanized, transmission-prone areas, similar to the US. Two, in all of these other countries, the onset of the pandemic (as measured by the date of their 15th confirmed case) *pre-dated* the US which means that they had *less* information to guide their decisions as to how to navigate the spread. Lastly, by scaling up their population sizes, we can compare deaths attributable to Covid-19 to match those of the US.

The University of Oxford has constructed a scale — a stringency index — based on 13 responses such as lockdowns, strict social distancing, testing volume, border & school closings, etc., to measure and compare how strongly a country responded over time. The 13 responses are divided into 4 indices used simply to record the number and strictness of government policies as related to public health, and are not interpreted as “scoring” the appropriateness or effectiveness of a country’s response or any resulting economic implications. The index shows that at 14 days from the date of the 15th confirmed case, the US response to the outbreak significantly lagged behind the other countries and was 25% of Australia’s, 23% of Germany’s, 18% of Singapore’s and only 15% of South Korea’s.

Because a virus spreads exponentially, this early delay in tangible measures — during an early window of spread — likely led to a drastic escalation in deaths. Over 115,000 Americans died in the four months following its 15th confirmed case. By scaling up the number of deaths in Germany to match our population, they would have suffered about 35,000 deaths or only 30% of our total.

The numbers appear even more dramatic for the other

countries. Australia, Singapore and South Korea would have experienced only 1324, 1358 and 1758 deaths, respectively, if their populations were scaled up accordingly.

These projections are further strengthened by the consistency of these projections using different methodologies. Two notable epidemiological projections, including one from Columbia University and based on theoretical models of transmission, have estimated that by instituting lockdowns just 2 weeks earlier similar reductions in the number of deaths from Covid-19 would have likely been attained in the US

Two major factors appear to be the main contributors and can be illustrated using comparisons with South Korea. First, less than three weeks of its 15th case, South Korea had closed schools, public spaces and had banned large gatherings nationally. The US response was disjointed with some states not issuing stay at home orders until 8 weeks (South Carolina April 10th) after the US confirmed its 15th known case.

Secondarily, its inability to perform adequate testing proved to be crucial. Three weeks after the 15th Covid-19 case, the US had only administered about 10,000 tests. By an equivalent point in its epidemic,

South Korea had performed 17 times more tests per capita than the US had done. This delay prompted delayed contact tracing efforts that may have allowed proper notice of hot spots and aggressive measures to stop their spread.

By mid-March, both countries had about 90 Covid-19 deaths. Throughout April, a total of 85 South Koreans had died for the month, while an average of 85 Americans died *hourly* during that same period.

Virus spread exponentially. The numbers will increase by 1.15-1.25 times daily from the previous day if allowed to spread unabated. This accounts for these steep curves we see and the need to “flatten the curve.”

Many excuses and rationales have been offered as to why the US death toll has been so staggering: Chinese duplicity and misinformation, the WHO, the failures of the Centers of Disease Control and Prevention, the media and many more. Yet other countries with the same information — or alleged misinformation — who undertook earlier and more decisive steps to quell the spread have seen vastly different outcomes. They now also are opening their economies sooner and more safely than the US.

This narrative is not to place specific blame or provide a

partisan view. It simply offers a comparative analysis of how responses to pandemics with exponential growth are scientifically and mathematically destined outcomes unless early and aggressive measures to stop the spread are instituted. This information may serve us well if this current wave continues to accelerate as expected or a second wave occurs in the future.

R. Delgado, MD &  
Staff