Dr. Delgado COVID-19 Update 08-21-20

Plasma Therapy Latest

The U.S. Food and Drug Administration (FDA) won't authorize the emergency authorization use of convalescent plasma (CP) to treat Covid-19 patients until more data about the treatment can be reviewed.

Studies conducted during previous viral outbreaks in regard to CP efficacy (SARS, H1N1, Ebola) often lacked control groups, meaning patients who got CP therapy weren't compared to patients who didn't, to see if it truly improved outcomes.

Both study recruitment and plasma donations/availability vary with the prevalence of COVID-19 in different regions, meaning that many clinical trials for CP often don't recruit enough participants to yield meaningful results.

No clinical trials have definitively shown that CP therapy helps coronavirus patients recover. Preliminary data for

several completed trials do suggest that those treated with CP therapy die at significantly lower rates, but the trials have not met the standards necessary for approval. Hopefully more data will emerge and the FDA may choose to grant authorization in the near future.

Saliva Testing

The Food and Drug Administration authorized emergency use this past weekend of a new and inexpensive saliva test for Covid-19 that could greatly expand testing capacity.

The new test, which is called **SalivaDirect** and was developed at the Yale School of Public Health, allows saliva samples to be collected in any sterile container. It is a much less invasive process than the nasal swabs currently used to test for the virus that causes Covid-19, but one that so far appears to yield highly sensitive results similar to those currently available.

In its preprint submission on the website medRxiv, which denotes it has not yet been peer reviewed or accepted into publication, it reports a greater than 94% agreement in testing outcomes when paired nasopharyngeal and

saliva specimens are obtained.

Yale's saliva-based test also skirts a step that other Covid-19 tests require: extracting the virus's genetic material. Extraction kits are one of many components of the existing diagnostic tests that have faced shortages. Supply issues have limited testing capacity overall, as well as slowed how quickly results can be returned.
The test can run samples in fewer than three hours in a lab, although the number could be much greater in larger labs with automation. Most importantly, it is inexpensive ($1-5/sample).

Moreover, Yale intends to provide its "open source" testing protocol to laboratories around the country. Other labs will be able to immediately adopt and implement the known method while using a variety of commercially available testing components that can reduce costs, speed/ turnaround times and increase testing frequency. And because the reagents for the test cost less than $5, the Yale researchers estimate labs should charge about $10 per sample, although that remains to be seen.

What have we learned so far?

Settings-Research has coalesced on a few key points about what types of setting increase the risk that an infectious person will pass the virus to others.

Essentially, the closer you are to someone infectious and the longer you're in contact with them, the more likely you are to contract the virus (time & dose), which helps explain why so much transmission occurs within households. Being indoors is worse, particularly in rooms without sufficient ventilation; the more air flow, the faster the virus gets diluted. Loud talking, heavy breathing, singing, or screaming expel more virus, which is why experts point to nightclubs/bars and gyms as risky businesses to be open. Everyday face coverings reduce the amount of virus projected, but aren't total blockades.

The reason having prolonged, proximate contact with someone is riskier is in part because there is a threshold level of virus you need to be exposed to become infected. This narrative augments the hypothesis that some people become sicker because they are exposed to higher initial dosing of virus.

Am I still contagious?-There was a lot of angst a few

months ago about some people who had seemingly recovered from Covid-19 infections continuing to test positive for the virus for weeks. Were they infectious?

It turns out this is an issue of testing itself. Most testing is conducted using a platform called PCR — polymerase chain reaction — that looks for tiny fragments of the Covid-19 virus. But the test can't tell if those sections of genetic code are part of actual viruses that can infect someone else, or fragments of viruses that are absolutely no threat.

It's clear now that people who had mild or uncomplicated infections shed active virus for somewhere up to 10 days after their symptoms started, but are likely not infectious thereafter.

Lingering effects-Name a body part or system and Covid-19 has left its fingerprints.

We know this: Unusually sticky blood can clog vessels on the way to the heart and inside the brain and lungs of infected people, causing heart attacks, strokes, and deadly pulmonary embolisms. There are growing worries that these and other health effects will be long-lasting.

Heart muscles can be weakened and increase the risk of future heart failure. Some data points to about 20% of people infected by Covid-19 suffering from some level of myocarditis or inflammation of the heart muscle. Atypical chest pain and “racing” hearts are also noted by many of those infected. This risk appears to be the predominant reason some football conferences chose to avoid their upcoming slate of games.

People whose first Covid-19 symptom might have been losing their sense of smell and taste may find this persists. Headaches and dizziness are also common. Mood disorders such as anxiety, depression, and PTSD follow in the wake of infections, and the mental confusion termed “covid fog” leaves people searching for words, struggling with simple math or memory deficits.

In July, a survey conducted by the CDC found that 35% of people who tested positive and had the common symptoms of Covid-19 — cough, fatigue, or shortness of breath — but were not hospitalized and had not returned to their previous health even three to four weeks later. Among those between 18 and 34 years old who had no previous chronic conditions, over 20% felt prolonged signs of illness.

More on asymptomatic spread-Key implications for the pandemic and trying to rein it in. Some percentage of infected people — roughly 25%, according to a recent review, though other studies have produced higher estimates — do not show symptoms at all.

Secondarily, whether or not someone is asymptomatic or pre-symptomatic, they can still spread the virus (though whether they spread it as efficiently as people with symptoms is still unclear). That is why public health directives continue to stress distancing, masks, and hand hygiene for everyone, not just people who feel sick. Once you do start showing symptoms and try to restrict contact with others, it is just too late to prevent exponential spread. Hence the concern with the upcoming school openings and the interval risk increase that creates.

Mutations to the virus haven't been consequential- Coronaviruses in general do not mutate very quickly compared to other viral families. This is a good thing. The leading vaccine candidates, for example, are based on the Covid-19 genetic sequence, so theoretically a major change could hinder the effectiveness of any vaccine. So far, that doesn't seem to have occurred.

What is still unknown?

Immunity duration-So far, despite some anecdotal reports, scientists have not confirmed any repeat Covid-19 cases.

All that supports the notion that Covid-19 acts like other viral infections. Researchers are finding that most infected people mount an immune response involving both antibodies and other immune cells that clear the virus, and that it persists for some amount of time. Reports of waning antibody levels raised some concern that perhaps protection to Covid-19 might not last very long (2-4 months) with big implications for the required frequency of required vaccine boosts. But immunologists have pointed out that antibodies for other viruses wane as well; their levels then surge upon re-exposure to the pathogen and they can still halt reinfection.

Researchers don't know for sure what quantitative level of antibodies are required to block the virus from gaining a foothold in cells, and how substantive a role pathogen-fighting T cells might have in fending off an infection.
In addition, people who recover from Covid-19 also

produce varying levels of antibodies. It's likely people who generate a weaker initial immune response might not be protected for as long from reinfection.

Who gets a significant clinical infection?

The sheer range of outcomes for people who get Covid-19 — from a truly asymptomatic case, to mild symptoms, to moderate disease leading to months-long complications, to death — is perplexing.

Scientists have postulated that a host of other underlying factors could help dictate why most healthy 30-year-olds shake off the virus after a couple days while some get severely ill. Many current hypotheses include genetic differences, viral load exposure, immunologic variances, blood types, etc.

Recent studies have pointed to another potential player. Perhaps up to half the population has immune-system T cells that were initially generated in response to an infection by one of the common cold-causing coronaviruses cousins and thus this facilitates some recognition of Covid-19 as well. These "cross-reactive" T cells could help give the immune system the boost it

needs to stave off serious symptoms, but researchers don’t know for sure.

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