

Remarks by Dr. Lawton Davis
May 20, 2020
Zoom Virtual Meeting
Skidaway Abigails and Skidaway Hamiltons

Thank you very much for inviting me to speak. Hopefully you will find it interesting and as I know I cannot cover everything, I will certainly attempt to answer questions at the end.

As a middle schooler, I had the opportunity to hear Francis Tarkenton speak and I still remember his advice on giving a successful talk: have an interesting opening statement, an interesting closing statement, and keep the interval between the two very short. I'll do my best to honor that, especially the interval portion.

What we now know as COVID-19 (CV19) was first recognized following the report of a cluster of unusual illnesses noted in Wuhan, China. It quickly became an epidemic in China, before making its way around the world in a matter of months and becoming a pandemic. But epidemics don't always become pandemics, and it's not always a fast or clear transition. For example, HIV was considered an epidemic in West Africa for decades before becoming a pandemic in the late 20th century. Now, thanks to advances in modern medicine, HIV is considered endemic, which means the rate of the disease is stable and predictable among certain populations.

Most viral pandemics have been caused by influenza (flu) viruses. Flu viruses can change from season to season and while health professionals are generally pretty good at predicting how the virus will change, occasionally a new virus pops up that doesn't behave as predicted. That's when a pandemic is most likely to occur because most people don't have immunity to the new virus.

Generally, people in the modern Western World feel that modern science has a pretty good handle on “germs” in general. We have antibiotics to treat bacteria, antiviral medications for some viruses, and vaccines to help prevent most of those for which we may not have an effective medical treatment. In fact, however, we have always been in a state of tension with a wide variety of germs. Some are very helpful, such as the trillions of bacteria that live in our guts; also known as our gut microbiome. There is all sorts of research being done regarding the gut microbiome; everything from how it's different in children born via C-section

rather than via the birth canal, to connections with mental health, gluten sensitivity, chronic fatigue syndrome, fibromyalgia and a host of other things. Other germs are obviously very harmful, even some of those beneficial gut bacteria, if they happen to be relocated elsewhere, such as into an open wound.

And a brief review of history documents evidence of severe devastation caused by a variety of germs.

The Plague of Athens

Around 430 B.C., not long after a war between Athens and Sparta began, an epidemic ravaged the people of Athens and lasted for five years. Some estimates put the death toll as high as 100,000 people. The Greek historian Thucydides (460-400 B.C.) wrote that "people in good health were all of a sudden attacked by violent heats in the head, and redness and inflammation in the eyes, the inward parts, such as the throat or tongue, becoming bloody and emitting an unnatural and fetid breath".

The Black Death: 1346-1353

The Black Death was a devastating epidemic of bubonic plague that struck Europe and Asia in the mid-1300s. The plague arrived in Europe in October 1347, when 12 ships from the Black Sea docked at the Sicilian port of Messina. People who had gathered on the docks were met with a horrifying surprise: Most sailors aboard the ships were dead, and those still alive were gravely ill and covered in black boils that oozed blood and pus. Sicilian authorities hastily ordered the fleet of "death ships" out of the harbor, but it was too late. Over the next five years, the Black Death would kill more than 20 million people in Europe—almost one-third of the continent's population. It was caused by a strain of the bacterium *Yersinia pestis* and was spread by fleas on infected rodents. Of course at the time they had no clue as to what was causing the illness and the bodies of victims were generally buried in mass graves. *Yersinia Pestis* is still with us and there are always a few cases reported in the US each year. Fortunately, we can now treat it effectively with antibiotics. This bacterium is one that is on the list of those that could be weaponized and used in a bio-terroristic attack.

(The plague changed the course of Europe's history. With so many dead, labor became harder to find, bringing about better pay for workers and the end of Europe's system of serfdom. Studies suggest that surviving workers had better

access to meat and higher-quality bread. The lack of cheap labor may also have contributed to technological innovation.)

Spanish Flu

The most deadly pandemic in history was the Spanish flu of 1918. The virus infected an estimated one-third of the world's population and was responsible for causing between 20 million and 50 million deaths. The virus didn't originate in Spain, but the country was the first to report on the outbreak, so people began calling it the Spanish flu (the Spanish thought it started in France and called it the "French flu").

There have been three other influenza pandemics during my lifetime: Asian Flu in 1957 – 1958; Hong Kong Flu in 1968, and the Swine Flu in 2009-2010.

The swine flu pandemic of 2009-2010 was caused by a new strain of the same virus that caused the Spanish flu — the H1N1 virus. The swine flu infected an estimated 700 million to 1.4 billion people, which was far more in absolute terms compared with the Spanish flu. But the mortality rate was far less, at an estimated 0.01% to 0.08%, or about 100 times less deadly.

Which brings us to our topic du jour, COVID-19

Think for a moment about what circumstances need to be in place for a pandemic to literally erupt on the world scene:

1. A susceptible population; in Epidemiological terms that would be a “naïve” population.
2. Would need a brand new germ;
 - a. Specifically a new germ that spreads very easily from person to person.
 - b. Even worse if it causes severe illness
3. Mix in a bit of western cultural Complacency – you know, we can handle anything...
4. Toss in the ability to literally travel the world in a matter of hours and you have the perfect recipe!

In describing the infectivity or contagiousness of a virus, Scientists talk about its Replication potential, or its R naught value. We'll just call it the R value and it describes, on average, how many secondary cases will develop from each primary case. (In other words, how many people I will give it to if I become ill). The greater the R value, the more contagious the virus.

And, for any R value greater than 1, the disease can spread exponentially.

We all know how quickly a typical flu outbreak (“seasonal flu”) can spread; for the sake of comparison, some common viral R values are noted below:

Seasonal Flu = $R \approx 1.2$

Spanish Flu: $R \approx 1.8$

Chicken pox: 3.7 – 4

Polio, smallpox, Rubella: 5 – 7

Ebola: 1.5 – 2

SARS: 3 – 4

Measles: 12 – 18 (the most contagious virus we know of)

Early estimates of CV19 R value: 2.2 - 5.7; depending on who did the estimate and where it was done.

The R value actually can change over time; as more people are infected with a virus and develop immunity, it becomes less likely that everyone who is exposed will develop the disease because many of them are no longer susceptible.

This introduces the concept of “herd immunity”. Charcoal fire....

With an R value of 2.2 or so, it’s estimated that we would need to have 80 – 90% of the population immune to CV19 in order to achieve herd immunity.

AS noted, a cluster of unusual illnesses was reported in Wuhan China in late December, 2019. It was quickly determined that the illness was caused by a new Corona Virus. (electron microscope – crown like appearance; Latin for crown is “corona”)

There are many other coronaviruses, most of which circulate in animals. However, at least 6 others have made the leap into the human population:

4 cause symptoms of the common cold

SARS (? Bats to civet cats to people in 2002?)

MERS (possibly from Camels; 2012)

Now, SARS-CoV-2: (? Bats?, maybe pangolins? Has also infected a tiger in NY zoo)

SARS-CoV-2

We’re not sure exactly when CV19 arrived in the US, but certainly it was here by mid-January. Seattle became an early hotspot.

First case in GA probably on March 2, 2020
First death in GA March 12, 2020

First case in Coastal Health District reported on: 3/18
First case in Chatham County: 3/20
First death in Chatham: 4/01/2020

Local statistics...

47% male, 53% female; 43% white, 52% AA, 5% other ethnicity; of the deaths, 71% white, 29% AA. 5 of the 16 deaths have been among NH residents.

In response to recognition of the emerging pandemic, local officials took several actions which at the time were quite controversial and largely unpopular:

On March 11, the Mayor of Savannah canceled our St. Patrick's celebration and parade, and subsequently the music festival which was to follow (along with many other events).

Between March 13 – 20, Chatham County, City of Savannah, and several other municipalities in Chatham County declared a state of local Emergency – limited the size of gatherings, closed some businesses, and instituted social distancing protocols.

This also happened all along the I-95 corridor; Camden County was particularly aggressive.

The Governor's initial Declaration was on March 23, 2020. He declared a state of Public Health Emergency; Co-Lead Agencies: GEMA and DPH. Actually, his Executive Order was a good bit less restrictive than most of our local declarations – loosened things here a bit. But helped elsewhere. In Chatham County, CEMA opened its Emergency Operations Center; we provided staff; CEMA managed daily operations, we pretended to be subject matter experts. It has really been a very nice partnership. There have been numerous daily or weekly calls and discussions with a variety of entities including non profits, hospitals (bed / ventilator counts, etc.), local law enforcement agencies, National Guard, and others.

After exposure to CV19 there is approximately a 14 day window for development of symptoms. It may occur as early as day 2, but is generally 4 – 6 days after exposure though it may be a full two weeks.

Initially, CV19 was felt to be primarily a respiratory illness and the classic symptoms were fever, cough, and sore throat. From the earliest days, it seemed to largely spare children but infect all other age groups, and to be particularly bad for older individuals & / or those with underlying conditions such as heart disease, lung / breathing problems, uncontrolled diabetes, or be immunocompromised in any way. Now we know it really doesn't spare children.

Over time it was recognized that some of those who were particularly ill and who might require ventilatory assistance, would at times seem to be improving, then suddenly deteriorate. And it was noted that many of these and others were developing blood clots (pulmonary emboli) - more than one would typically expect, even in one who is at forced bed rest on a ventilator (those are already at high risk, but CV19 seems to make it even worse...).

It is now recognized that in some people the virus seems to preferentially infect endothelial cells – those lining our blood vessels; perhaps this leads to the development of blood clots.

It may also be a factor in the Pediatric Multisystem Inflammatory Syndrome (PMIS) which is felt to somehow be related to an “overactive immune response”; sort of like a combination of Toxic Shock syndrome + Kawasaki's disease.

Suffice it to say that the spectrum of illness caused by CV19 is quite broad. It's estimated that somewhere between 25 – 50% of people have either no symptoms or symptoms that are so mild as to be virtually unrecognized. At the other end of the spectrum is severe illness and death. And as we learn more there are other manifestations being recognized – loss of the sense of taste or smell; unusual rashes, even diarrhea as a presenting complaint. Our local epidemiologists are convinced that the most common symptom reported in those we have investigated is simply a bad headache for which there seems to be no reason (no hangover, no history of migraines, etc.).

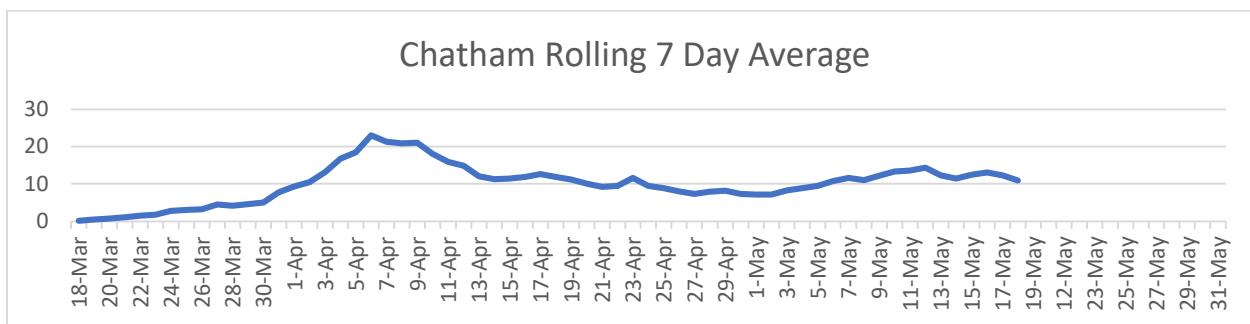
We also know that CV19 is capable of sneakily spreading silently throughout certain populations as supported by several studies of those on cruise liners and a US aircraft carrier. These studies verified that a large percentage of people onboard were positive for the virus despite being asymptomatic.

Nursing home study: 1st positive – tested everyone; 64% positive (57 patients). 56% of the positives were asymptomatic. 15 of those died (26%).

This is why we consider a single case of CV19 in a NH resident to constitute an outbreak and recommend testing of all residents and staff. One of several “worst case scenarios” is to have a healthcare provider infected with CV19 who is asymptomatic and works in several different facilities, especially if they are long term care facilities, or some other congregate living facility (e.g. prison). In fact, we are dealing with this exact situation locally, right now.

So where are we, how have we done as a community, how can I protect myself and my family as “the economy reopens”, and how will we ever emerge from this pandemic?

Early on there was a lot of talk about “flattening the curve”; basically limiting the size of our local epidemic such that we did not overwhelm our healthcare system. Remember, just because we’re in the midst of a pandemic doesn’t mean that other illnesses and trauma don’t continue to occur.



Rates of cases per 100K population are generally lower along the I-95 corridor than in many other areas of in the state. Chatham County has an airport, two interstates, a major seaport, bus and rail service, as well as a tremendous trucking volume related to the port; it is also the 5th largest county in Georgia by population yet is #20 in number of cases. The Coastal health district encompasses the entirety of the I-95 corridor in Georgia, is the 8th largest in the state by population, 8th out of 18, yet has the second fewest number of cases; only the Dublin district has fewer; population of that 10 county district is about half of Chatham County, alone.

All of this suggests that we have flattened the curve – that’s the good news. The flip side is that that means we likely have limited the numbers of people who have been infected and subsequently recovered from CV19, thereby limiting or slowing our development of herd immunity. That means that there are still a lot of people out there in that previously described “naïve population”.

It is obviously very important to understand exactly how the virus affects people, and how best to support and treat someone who is infected. But it is also very important to understand how our immune system responds to an infection, and how such response may guide development of better tools to treat and prevent future infections.

So let's talk about Antibodies, Immunity, Treatment & Prevention, and ultimately what will need to happen to emerge from this pandemic.

Among the many unknowns about this particular virus, one of the most vexing is whether or not infection and subsequent recovery actually confers immunity to reinfection. Our history with other Coronaviruses is mixed, at best. Those 4 known to cause "common cold symptoms" seem to be able to return year after year, sort of like the seasonal flu – that is, no lasting immunity develops.

Studies have documented protective antibodies that appear fairly early on during infection with SARS. However, those antibodies appear to wane, largely being gone by the third year; so maybe we're protected for ~ 2 – 2.5 years.

Currently, there are no studies that support the evidence of immunity to reinfection to CV19 in humans. However, there is some very recent, very encouraging news... we know that people do mount some immune response because the vast majority of symptomatic people get well. Recently, studies have documented the development of the type of antibodies that should help protect us against reinfection. Equally important, the development of these particular types of antibodies should also allow for the development of effective vaccines. Without getting too far out into the weeds, this virus has a "spike protein" – you've all seen cartoon representations of the virus looking sort of like a WW2 floating mine; spherical with little spikey projections all over it. The spikes are what somehow attach to receptors in human cells and allow the virus to gain entry. Neutralizing or blocking antibodies produced in response to infection, or induced by a vaccine, would attach to those spikes, altering their shape or chemistry, thereby precluding their attachment and rendering the virus basically harmless.

Recently (published within the past week) there has also been documentation that two other types of immune cells also show a robust response. You may have heard of helper T-cells and Killer T-cells from discussions about HIV; or maybe you've heard of CD4 & CD8 t-cells. It has been shown that people who recover "normally" from an infection with CV19 show a robust development of these t-cells, which is typical of a good immune response to any virus. And hopefully

these t-cells will also be induced by vaccines that target the spike protein. The helper t-cells augment the production of immunoglobulins (antibodies) by B-cells (another or our immune response cells). The killer t-cells somehow recognize our human cells that have been infected by the virus and kill those cells, shutting down viral replication. There is also a very recent report from China where an investigator extracted certain antibodies from the serum of people who have recovered from CV19. He infused some of these antibodies into mice that were infected with CV19 and they recovered promptly; he also infused those antibodies into a different set of mice and then attempted to infect them with CV19 – and they were immune! An even more recent study in monkeys tested a vaccine; one group of monkeys was vaccinated, another group was not. The vaccinated group did not become infected when intentionally exposed whereas the other group did. (there have been a couple of other, similar studies, but this is the first that has been “peer reviewed” – basically validation that it has undergone scrutiny by experts other than the ones who did the study and the conclusions are deemed valid.)

All of this is very encouraging news. Let’s hope that this experimental data, and some other “petri-dish” experiments supporting this stuff, actually translate into a nice protective immune response, and also allow for the development of a safe reliable vaccine. However, on a cautionary note, recall that HIV has been with us in the US since at least 1981. Humans develop all sorts of antibodies vs. HIV – and are the basis for rapid screening tests. However, none of those antibodies are protective against reinfection, and after 35 years we still do not have an effective vaccine.

Regarding effective treatment, there are multiple trials underway evaluating the efficacy of several different therapeutic interventions. These include antiviral drugs, anti-malarial medications (that you’ve all no doubt heard about), Monoclonal antibody therapy, infusion of plasma from patients who have recovered, and other immune-modulating medications – or sometimes a combination of therapies or a cocktail of antiviral meds as is commonly used in treating HIV patients.

Although having some theoretical benefits and thus giving rise to overhyped enthusiasm, Chloroquine and Hydroxychloroquine have failed to demonstrate any clear-cut benefit and may actually be harmful. To their early credit, in the almighty petri dish, hydroxychloroquine especially seems to inhibit CV19 viral replication; and hydroxychloroquine has a potent anti-inflammatory effect - that’s

why it's used to treat some auto-immune diseases such as Lupus. Unfortunately, both drugs also have the nasty habit of inducing cardiac arrhythmias that can lead to death. Studies are ongoing.

Perhaps the most hopeful medication currently undergoing tests is Remdesivir, an antiviral drug developed as a potential treatment for Ebola. It didn't pan out for Ebola, but it seems that it may actually benefit some people infected with CV19. Trials are underway. Georgia has received some of the drug and it has been distributed to some hospitals around the state. More will be going out on today. None of our local hospitals received any of the initial allotment but we do have some available in Savannah should physicians elect to treat anyone with it. (The distribution was based on numbers of critically ill CV19 patients / on vents / ECMO). (Extra Corporeal Membrane Oxygenation – basically a “heart lung machine”).

So how will we ever emerge from this thing?

In order for that to happen, at least one of two things must occur.

We must either develop an effective treatment for the virus, or we must develop herd immunity, or both. As alluded to previously, the only two ways of developing herd immunity are to become infected, recover, and in the process develop protective antibodies, Or to develop an effective vaccine. So, as we currently are not assured that we have either an effective treatment or the ability to develop immunity by recovering or via a vaccine, what can we do?

Well, we really have only a couple of tools available to deal with this thing, and neither is particularly high tech or sexy.

One is social distancing combined with other good public health hygiene practices. The other is widespread, appropriate testing, with prompt reporting of results combined with aggressive case investigation, contact tracing and appropriate quarantine or isolation practices.

Testing has slowly become more widely available. The gold standard is the RT-PCR test performed by collecting a NP specimen. The naso-pharyngeal swab test for COVID-19, has a theoretical specificity and sensitivity of basically 100% for both. That means that in a laboratory-controlled environment, if the test is negative, it's 100% certain that that person is not currently infected with CV19. If positive, it's 100% certain that the patient DOES have CV19. Those numbers are reproducible in a very controlled environment.

In the real world, swabs are taken from someone sitting in a car by a clinician reaching in through the window, packaged, refrigerated, then shipped either that evening or the next day to a lab. If the lab isn't to run the specimen within 3 days of collection, it must be frozen to retain viability. Unfortunately, packages get lost or mishandled from time to time; technicians may not process them correctly 100% of the time; or the collection itself was not great.

So, in the real-world experience, what I'm reading is that we can assume a 10% false negative rate, *at least*; and it really is much more likely to be in the 30 – 40% false negative range. However, a positive test would still be just that – positive (unless the lab mixes up a specimen label).

It is also reassuring that the RT-PCR test being used does NOT cross react with other common “bugs” that might be found in the nasopharynx / throat of individuals, including those other common coronaviruses that cause the common cold type symptoms. So, a positive is truly a positive (that's the 100% specificity measure). The sensitivity is dependent on the care with which the specimen was collected by the clinician and handled both prior to and after arrival in the processing lab.

Unfortunately, I'm not sure the same can yet be said for all those antibody tests out there. I am certain that good reference labs can approach that same benchmark on specificity and sensitivity, but the rapid ones currently in local offices / urgent care centers likely do not meet those standards and the FDA has admitted as much. So, at the moment a serum antibody test is not recommended as a diagnostic test for CV19 as the test may show a positive result because it is cross reacting with some other coronavirus, or something else entirely. And, as noted earlier, we do not know that the presence of antibodies confers immunity. So if one has a positive test with one of the tests currently available, we cannot be certain you have, in fact, had CV19 or that you are immune. Therefore, utilizing an antibody test to determine that someone is ok to return to work really doesn't make good sense – yet!

Now, having just cast some serious negative shade at antibody testing, it is likely that it will actually become very important in the near future. There are reliable serum antibody tests and these will no doubt become much more widely available in the not too distant future. And assuming the encouraging research data discussed earlier holds true, and we do in fact develop at least some decent short term immunity, a rapid serum antibody screening test similar to what is used for screening for HIV would give us a true picture of the percentage of people who

have been infected and who are immune – in other words, we could actually determine our level of herd immunity and be fairly certain that it is in fact safe to get back to some level of normalcy. You may also hear the term seroprevalence; basically exactly what we've just talked about; the number of people whose serum is positive for antibodies to CV19 (and hopefully meaning that they are immune to reinfection).

So, as we deal with reopening society, and it will no doubt be reopened, we each will face some important decisions. I would urge you to be cautious in your activities. The fact is that we're still under a shelter in place order for those of us over 65 or who have underlying risk factors; and we're still encouraged to wear a face mask or cloth covering when out in public. I would remind you that just because it may be "ok" to engage in certain activities, there's no requirement that you must do so. And we know that certain types of activities carry a higher theoretical risk of exposure / transmission than some others. Here's why...

A person infected with CV19 exhales a very small amount of potentially infectious "aerosol droplets" during normal respiration and a bit more with normal speech. Coughing and sneezing expels a significantly greater amount and at speeds that allow the droplets to travel much further. Singing also is associated with a high volume of aerosolized droplets. In fact, anything that causes deeper breathing such as exercise, or even playing an instrument in a concert – say a violin requiring quite a bit of exertion – would lead to an increase in droplets being exhaled.

To become infected, one must inhale an amount of viral particles known as the inoculation dose, or minimum infective dose. We don't know exactly what that number is, but we do know that achieving such an infective dose is a function of the amount of infected droplets being inhaled and the duration for which they are inhaled. So, sitting next to someone and speaking face to face would generate low levels of aerosolized droplets; a very brief interaction would quite likely be safe. But chattering on for 15 – 20 minutes would quite possibly allow one enough time to inhale enough particles to become infected. Of course, the further apart the two are, the lower the level of exposure, as well. Thus the "within 6 feet for 10 – 15 minutes" rule for determining who might be a "close contact". If you're out on a walk and someone jogs past, sure, they're exhaling more droplets, but the time of exposure is extremely brief, you're outside in fresh air, and the likelihood of becoming infected is very very low.

It would be instructive to review a couple of clusters that have been well documented and actually mapped out. Restaurant; Call Center

Most of you have read about the choir out in Washington; the so called Skagit County Choir practice. 61 people attended a 2.5 hour rehearsal; used their own music and somewhat socially distanced. It was later determined that one person was symptomatic though that person didn't really think so at the time. There were 32 confirmed and 20 other suspected secondary cases; 3 were hospitalized; two died.

So, situations where you are in an enclosed space breathing "community air", especially for an extended period of time, and especially if you or someone else is engaged in loud talking or singing, would constitute relatively high risk venues. Think indoor restaurants, certain workspaces, and especially church services. Should your church decide to begin meeting in person, please don't even *consider* sitting in the choir loft with your fellow singers.

There is also a concern about "intergenerational gatherings" – mixing children with seniors. Most infected children are asymptomatic but can still spread the virus to grandpa or grandma....

It is true that we may well have peaked in Georgia but this virus has not yet left us; and achieving the peak in no way equates with reaching the end – it doesn't just simply stop. Be safe, be smart, and be careful.

In the mean-time, scientists will continue to work on medical therapies and the development of vaccines. And other studies will also be ongoing (e.g. recent observational data showing a correlation between serum Vit. D levels and severity of disease. Basically the lower the level of Vit. D, the more likely a severe case of CV19). Also, government entities will no doubt become very creative in facilitating the opening of certain businesses while allowing for maximum safety – such as closing streets to allow more outdoor space for restaurant seating.

Quite a few people have asked why we seem to have fared a little better here along the coast than in some other areas of Georgia. I believe there are three factors that contribute to this: one is the early action taken by elected officials to cancel many events that would have attracted large crowds and also people from other areas of the country, coupled with early closure of certain businesses and promoting social distancing. The second is that we have been fairly successful in aggressively pursuing case investigation, contact tracing, and issuing quarantine or isolation orders as appropriate. And finally, and maybe most importantly, I believe we've basically been lucky. There have been several instances that easily could

have triggered a cluster of cases but in each instance we seem to have dogged the bullet.

We're still dealing with a largely unknown virus and things are changing rapidly. We can each make intelligent decisions to continue to practice social distancing, wearing a mask when out in public, and avoiding gatherings where social distancing is difficult to maintain.

Thanks

Notes:

Covid19.gachd.org – our local Coastal Health District web page. The graphs are based on the date a test is reported as positive, not the date of symptom onset or the date it was collected; so it's really a blurry snapshot of what was happening 5 – 7 days ago.

Follow this link to see the Dept of Community Health CV19 Nursing home report:
<https://dch.georgia.gov/announcement/2020-05-20/long-term-care-facility-covid-19-report>