To my valued patients

We live during truly amazing times

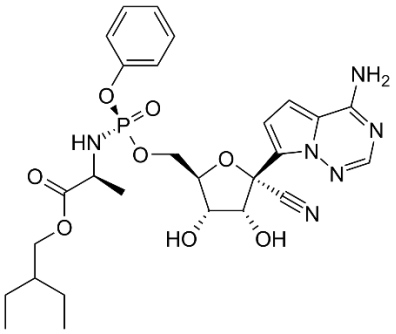
It's amazing if you think about it. We are seeing an entire science evolution at hyper-speed. The world was introduced to a new, never before seen virus at the end of 2019. The genome or the genetic code for SARS-CoV-2 was sequenced at the end of January of 2020. The first vaccines were literally injected into patients at the end of March. Think about what I have just said. Weeks after discovering the virus, the genome was sequenced and just a little over 60 days later test vaccines were all ready to be administered to patients. I think sometimes we take our technology for granted. We are so used to immediate satisfaction - from Amazon deliveries to internet connections - that we can no longer truly understand the wonderful effort this represents. It is an amazing collaboration between virologists, microbiologists, geneticists, biochemical researchers, medical researchers, and medical clinicians.

The scientific effort directed toward developing antibody testing and a vaccine for the novel coronavirus is a remarkable coalition of individuals, corporations, universities, and governments. Take a moment to recognize the tremendous effort of the entire healthcare field - medical doctors, nurses and therapists, bench scientists and technology workers - to bring such a miracle to fruition. Instead of seeing our differences, be thankful of our harmonies. We live in amazing times and in an amazing country.

More good news about remdesivir

At the University of Chicago School of Medicine researchers have stated that they saw "rapid recoveries" in 125 patients taking the experimental drug remdesivir. The university recruited 125 people into two phase 2 clinical trials. All patients, of whom 113 had severe disease, were given daily infusions of remdesivir. Most of the patients who got the drug have been discharged! Two patients died. Similar trials are being run concurrently at other institutions, so we don't have conclusive results yet. Data will soon be released on the first 400 patients. A word of warning, I do not have access to the actual study

which, as of this writing, has not been published. Second, there was not a control group or placebo group to compare against.



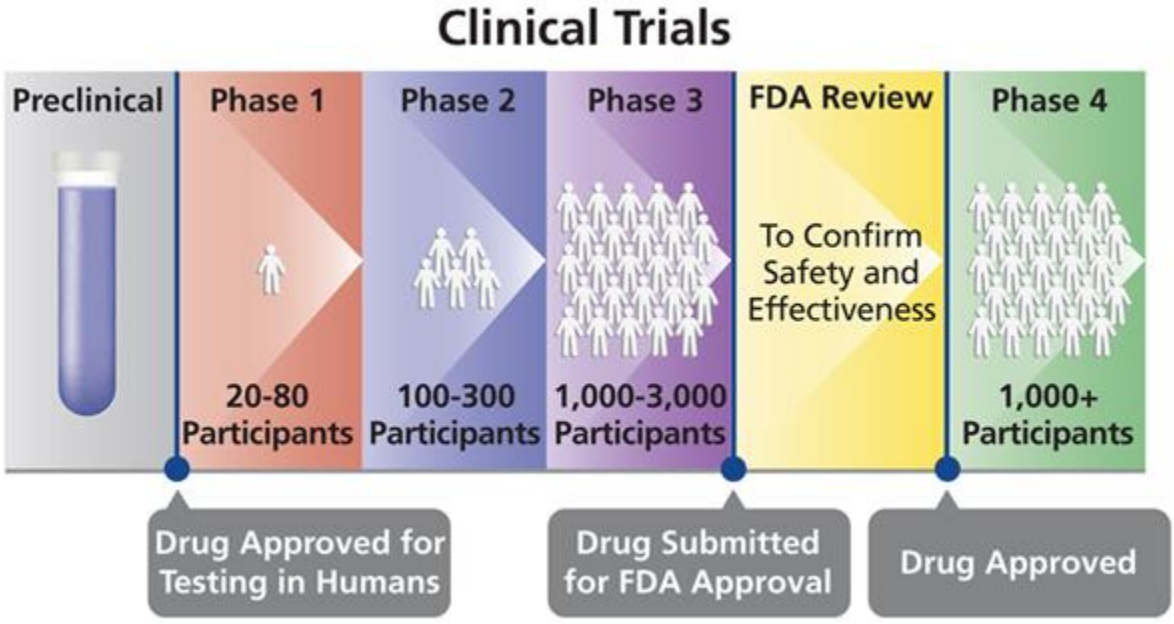
The chemical structure of remdesivir

Comments by one investigator were heartening though. She said that as patients started the drug, the fever curves started falling; people were able to come off ventilators a day after administration. Most of her patients had severe disease and frequently left the hospital after 6 days.

Gilead, the maker of remdesivir, has several ongoing studies of the drug. One study is evaluating 2400 patients at 152 sites all over the world with severe COVID-19. Another study is looking into patients with moderate COVID-19 disease and includes 1600 patients at 169 different centers. There is a lot of "action" surrounding remdesivir.

A cheat sheet of medical trials

With all these trials coming out, you may need to start learning the lingo of drug trials. Below is a cheat sheet for you to use when reading newspaper articles or information on the internet.



Phase 0 (preclinical) is usually a very small initial study, consisting of less than 15 people. In preclinical trials, a very small dose of medication is given before initiating trials with the dose for which approval will be requested.

Phase I is a slightly larger study of usually 20-80 people who have no underlying conditions. The goal is to calculate the maximum dose which can be safely administered without side effects and to determine the best route of administer (i.e., oral, injection, infusion).

Phase II is a larger study involving up to 300 individuals who have the medical condition a new medication is intended to treat. The goal is to evaluate how the new medication works in comparison to previous medications for the same condition or in comparison to no drug if the treatment is for a disease that no treatment exists. The data collected during Phase II trials helps investigators plan the methodology for Phase III trials.

Phase III is usually double blinded (neither the doctor nor the patient knows which drug the patient has received) and is study of up to 3000 participants who have the condition the new medication is meant to treat. Some trial participants are randomized to the new treatment while the remaining trial participants are randomized to an older treatment or to no treatment. Randomization helps eliminate bias when interpreting results.

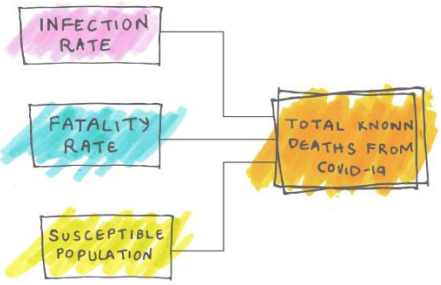
If investigators demonstrate that the new medication at least as safe and effective as the old medications on the market, the medication is ready for FDA evaluation and approval.

Phase IV occurs after the drug is on the market and more information is acquired from a population of users of the medication.

The news reports of potential new Covid-19 treatments may mention what phase a trial is in. Armed with the information above, you will be able to know where in the development scheme the drug is.

Another sign of lower infection mortality rate

I found an article not yet in print that was interesting. Since it is in "prepublication" it has not been certified by other scientists who have reviewed the results and deemed them reliable. The researchers tested antibodies to SARS-CoV-2 among residents of Santa Clara county. They sampled 3,300 individuals whose characteristics were adjusted for zip code, sex, and race to truly reflect the demographics of Santa Clara county selected. The prevalence of positive antibodies was found to be 2.5-4.2% or an estimated 48,000 to 81,000 people as of early April. I can hear the yawn coming out so let me tell you why this is so interesting. The numbers they found were 50-85 times the number of reported confirmed cases.



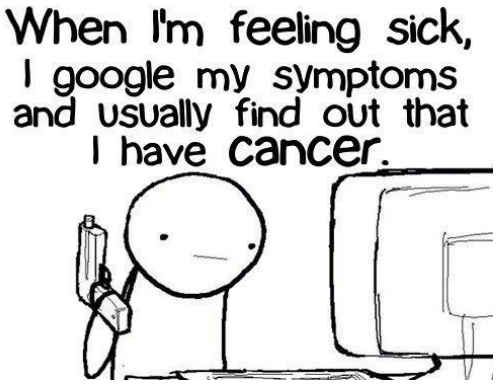
This means there are tons of people out there who had almost no symptoms yet had exposure to the disease. Please look at the equation in red below. If the number of infected fatalities is divided by the total infected to determine infection fatality rate and if we just use the number of "known" symptomatic cases, the denominator is small, and the Infection fatality rate is high. But, if we now include all these estimated asymptomatic cases, suddenly these silent cases have increased the denominator markedly by a factor of 50-85 and dramatically reduce the calculation for the fraction of people dying. For example, if we test only symptomatic people which is mostly what we are doing now and 2 out of 100 symptomatic people die, the infection fatality rate is 2/100 or 2%. But if there are 50-85 asymptomatic people not usually test who were infected the infection fatality rate is actually 2/5000 to 2/8500 or .04% to .023%

Infected Fatalities = Infection Fatality Rate (instead of 2/100 dying, we may have 2/5000-2/8500 dying)
Total Infected

I get it, but I do not get it

A major crisis frequently results in people ruminating about the crisis. These ruminations result in going down the rabbit hole of worse outcomes and into the valley of despair. Our equilibrium is disturbed we immediately start wondering about all the terrible things that could happen. Panic sets in before any possible bad outcome can even happen.

I see this a lot in my office, especially when patients refer to the internet to try to diagnose their symptoms. A person with a sore throat, for example, looks on the internet for causes of a sore throat. Possible cause numbers 1 to 99 have to do with viruses or bacteria or allergies. Down there at the bottom is cause number 100 and the one that is least likely to occur - cancer. So, the patient makes an appointment because he/she is concerned that his/her sore throat is cancer. I am not making fun of anybody, but to a greater or lesser extent, we are all built that way. I guess it's just the way we are genetically designed.



Similarly, I believe people are taking this approach to the coronavirus. The uncertainty and unknown genetically causes our mind to seek out the worst possible outcome.

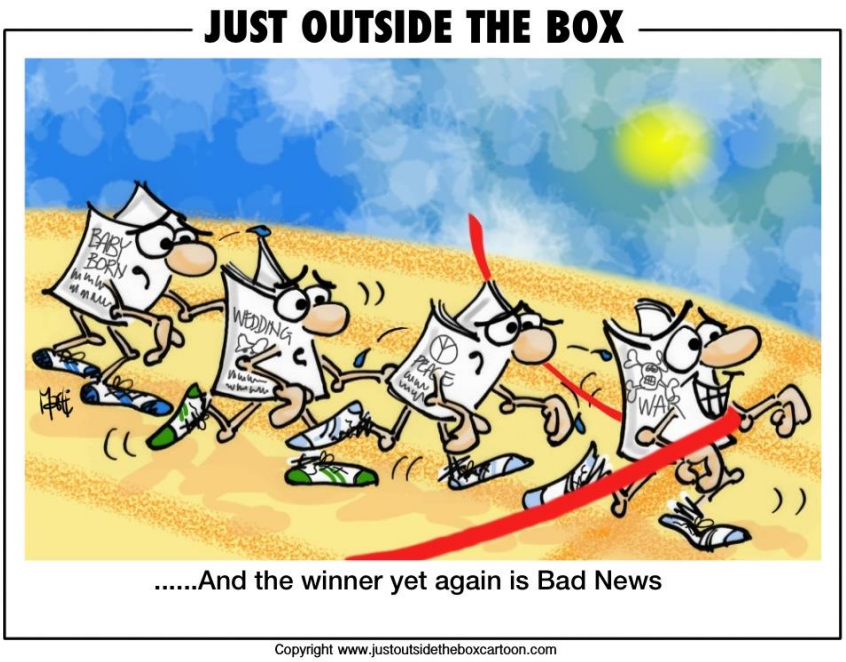
This virus will not be the end of life as we know it, as the naysayers proclaim. It will not end the glorious experiment we call democracy in America. America is showing its strength in how we come together to fight this virus, despite the forces trying to tear us apart. This nation has survived a revolutionary war, a civil war, 2 world wars, numerous epidemics and financial depressions and recessions. This is yet another problem we will overcome. You can count on it.

Bad news sells

Working hand in hand with assuming the worst, is the concept of bad news sells. It is said that bad news travels at the speed of light and good news travels like molasses, for a reason. Are you going to watch a report on Sally Jones finishing high school or John Smith being brutally murdered? Now enter in the 24-hour cable news cycle. Because of huge number of hours of needing information, you can hear all the gory details about John Smith's murder and talk about it with all your friends who have watched the same news as you.

The same is true of COVID-19. Everyone is stuck at home and all they hear is bad news: NY does not have enough respirators, 800 people died of the disease today, we have no sure cure.

Of course, in our society there simply must be someone to blame. Things don't just happen, there must be someone to fault. So, in comes finger pointing. People of similar beliefs point to another group and say, it's all your fault. The other side answers, its not out fault, you are at fault. And so, the cycle continues.



We are not going to handle this crisis perfectly. No one will make every decision correctly. I believe that almost everyone on all sides is really doing their best. They may not agree, but we need to stop assessing blame. I don't necessarily agree with Henry Ford a lot, but when he said, "Don't find fault, find a remedy", I must agree.

If we stop immediately presuming the worst and we truly stop pointing fingers, we will all handle this coronavirus crises with thought, calm and reason. Each fatality is a loss, it ends the life of the stricken and tears into the soul of their loved ones. But death is inevitable. No one can avoid it. Previous generations experienced high rates of infant mortality and shorter life spans. We have forgotten how vulnerable we are. Science and technology have spoiled us. This pandemic is a strong reminder that we are mortal. But, ultimately, in the last 70 years we have developed amazing tools to treat any number of diseases and we are just about to conquer another disease. There will be casualties in this war, but we are winning.

Medicine and Art (music again)

Sergei Rachmaninoff suffered severe depression almost his entire life. His symptoms were first noted after the death of his idol Tchaikovsky in 1894. For years, he just tried to live with it. When his first symphony was released, and deemed a total disaster, he went into a downward spiral during which time, he barely composed and rarely performed. His depression worsened and his family finally stepped in. In early 1900, his aunt suggested he try a new treatment developed by Sigmund Freud called psychoanalysis. Rachmaninoff went to see a therapist named Nicolai Dahl and was subsequently able to resume composing as well as play his music in front of live audiences (his piano concerto no. 2 is one of my favorites). Despite therapy he continued to struggle with periods of depression interspersed with bouts of intense activity.

After Rachmaninoff fled Russia in 1917, he composed only six original pieces during the remaining 25 years of his life. He lost nearly everything in the Russian revolution, so he tried to restore his family's income by performing as a piano virtuoso. In 1934, the then 61-year-old composer was struck with inspiration and began "working literally from morn to night" to complete a masterpiece (perhaps he was bipolar). Like Brahms and Liszt before him, he was inspired by a simple tune by violin virtuoso Niccolò Paganini. Thus, he composed what is one of the most endearing pieces or a Rhapsody on a Theme of Paganini.

I cannot recommend this piece enough. This video even gives you a brief explanation of the piece, so you enjoy it. To receive the complete explanation of this rhapsody, please start the video from the beginning if by chance it accidently begins somewhere in the middle. Sit back, watch, and just listen.

https://www.youtube.com/watch?v=c33q87s03h4

As usual, thank you for reading this newsletter

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