

STICKY WICKET

Corona L. So, what have we learned?

Mole

Original artwork by Pete Jeffs - www.peterjeffsart.com

Hey there! I'm in *such* a good mood; I hope you are having a good day as well. Yesterday, I gave an actual, in-person seminar at a university in *another city*, and then when out for a really nice dinner with Dolphin and Lynx. Then I came home, and like magic, leaves sprung out on trees and oxygen filled the air. Okay, pollen did as well, so I am a bit stuffy, but hey, it really is Spring! (Remember, I live in your past, so give me some leeway here, please?)

So, this is the fiftieth Corona File. Fifty! When I started to write these, I had no idea that I would be still writing more than two years later. Okay, yes, there were many scientists who said that it would likely be more than one and a half years before we were out of this. And yes, I know that we are *still* not out of this. BA2 is surging in Europe, and now the Eastern U.S. China is struggling to get to zero COVID. And large parts of the population are waiting for vaccines, or not wanting them, ever. Ever, ever. Never. Okay, we get it. Meetings that were postponed and postponed again seem to be back on the schedule (although we remain wary of scheduling anything in the next winter months, for fear of the next wave). We are traumatized. We are also, many of us (me, included) back to worrying more about grants, papers, bad reviews, and troublesome

experiments than about public health. It might be a good time to stop and think about what we have learned from all this.

Here's the thing. Whatever I say about what we have learned (or not learned) you will likely disagree with me. That's because (a) you are very smart, and (b) scientists like to argue (it's what we do). So, despite the title of this, Corona File #50, I'm not going to talk about what we have learned. Instead, I'm going to talk about what *I* have learned. So there, you can't argue that I'm wrong. Okay, you can certainly argue that I'm foolish, stupid, ill-informed, misinformed, arrogant, unappreciative, and prone to exaggeration. But I'm not. Okay, I'm prone to exaggeration, but not the other things. Except maybe foolish; I'll give you that one, too.

The following is my list of what I have learned from all this. Hey, I'm the Mole. I do lists.

1. We were not ready for this

Of course, we were not ready for a pandemic, despite decades of warnings. But I had little idea of how unprepared we were as a society (or many societies). Since I am talking about what I learned,

it was how very unprepared I was. My institution locked down in March of 2020, and I remember my assistant marveling at my suggestion that it could go on for not just weeks, but months. I also remember the discussions and concerns that we would not be able to identify enough infected individuals to have a cohort for clinical studies. Some of my colleagues had no doubts, but I don't think any of us expected more than two years of impact. I was unprepared for the hit on my lab's research; I was unprepared for the emotional toll on myself, my trainees, and others who I am close to. But I want to point out another way I was unprepared.

Early on, within days of our lockdown, we began working on testing. I figured that 'hey, this is exactly the sort of thing we do, the identification of molecular species, and we are good at it.' We obtained a couple of kits from China, and quickly compared them to our home-made tests (even using home-made recombinase). We also included controls that were missing in the tests, such as a control that would tell us that the input materials (the swabs) were of sufficient quality. Simply put, the tests worked great. But I was completely unprepared for the pushback I received from our clinical colleagues, that our tests were invalid and could not be used (other than for research). Now, I do understand the needs of clinical laboratories for formalized, standardized, and approved testing as a basic requirement (although I pointed out, repeatedly, that organizations make decisions based on drug testing, which is not performed with such requirements). Within a few more weeks, clinical testing was in place, but I was unprepared for the fact that our test for controlling the quality of the swab never made its way into practice. A kit from a company was deemed far more reliable than anything a research lab (even *my* research lab) could provide. What can I say? I learned something about the gulf between research and medicine. Please don't flame me – as I said, I learned. But as for preparedness, I'll get back to that.

2. *Science is great at figuring things out, less great about doing something about it*

Thanks to the remarkable efforts of scientists in China, we knew the sequence of SARS-CoV2 before anyone was infected in the town I live in (in which I live. Sorry). We also knew, from work on coronaviruses, how it infects cells. We quickly learned a lot about how this virus interacts with hosts to produce pathology. And recently, we have figured out (by 'we' I mean the community, not my lab) why some of the SARS-CoV2 infections impact smell. All of this is remarkable, especially the last one, since the project could not have even started until we knew that symptom. Such things often take years of careful study, but this was really fast (okay, we have to wait and see if 'we' got it right – really, the folks who are working on this are doing a great job).

We also managed to generate and test vaccines in an incredibly short time, thanks to remarkable work spanning decades on mRNA and adenovirus vaccines. We found out that we can speed up the

process of vaccine development when we need to, and that is a good thing. Many also learned that science is really important, but you and I already knew that (and you are very smart).

A bit more slowly, but very quickly, we developed antivirals and monoclonal antibody treatments. We knew how to do that, but still, well done.

So why do I say we are less great at doing something about it? Look, we got incredibly lucky. There was no hard evidence that a vaccine would work (we still do not have a vaccine for another coronavirus that infects cats). There was some reason for concern that a vaccine would actually make things worse (this is a problem called antibody-dependent enhancement; look it up if you're interested. It's a big problem). If that had happened, our next recourse would have been the therapeutics, and there is every reason to expect that if these went into wide usage, therapy-resistant strains would quickly emerge. And I'm not sure that we would figure out what to do about it.

And of course, none of our terrific research and engineering could solve problems of vaccine distribution or vaccine denial. We are getting better at the first one (but there's a long way to go) and I don't think we will ever solve the second one.

In Star Trek (and all of its spin-offs), and in many not-Star-Trek movies (like *Outbreak*), identification of the problem quickly, usually in hours, results in effective treatments, highlighting how important science is for solving major problems. (Okay, there is an especially bad episode of Star Trek: The Next Generation, or TNG for you Trekkers, where Dr. Pulaski stops an epidemic of 'evolutionary regression' that was turning crew members into various animals, which she fixed by expeditious use of a 'synthetic T cell.' Apparently, their science advisors were out that week.) Science (or medicine) doesn't work in this time frame. Getting where we are in just a couple of years is mind-blowing. (This is where I should probably transition into an ode to how, by working together, we can dramatically advance our knowledge and understanding of complex problems. And while I was very happy to see that happen, and while it was something I learned, it did not make the cut for this list. Because, (a) I already knew that, and (b) as near as I can tell, this applied only to the Terrible Pandemic, and only so far, and not to other complex problems, so 'we' haven't learned anything. Hey, it's *my* list.)

But now people who have been vaccinated, boosted, and boosted again are getting infected, and while they are not dying (a very good thing!), they are getting sick, losing work, and feeling pretty horrible. Efforts are underway to make an Omicron vaccine, but to date, effectiveness does not seem to be any better than the vaccines we already have. If we have hit a 'brick wall' (and I do not know that we have), we may find out why, but not know what to do about it. We're going to have to see.

Oh my, I see I only got to two items on my list. I guess there will have to be a fifty-one. That's okay, I would miss you if we couldn't get together. At least, one more time.

Until then! And yes, now I'm going to have some 'tea.'