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Five years of the COVID-19 pandemic: An interview with Dr. Arijit Chakravarty

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The World Socialist Web Site *spoke with Dr. Arijit Chakravarty on the current state of the COVID-19 pandemic and public health five years after the initial outbreak of the SARS-CoV-2 virus in Wuhan, China. Chakravarty is the CEO of Fractal Therapeutics, a science services company based in Cambridge, Massachusetts, that "offers model-based drug discovery and developmental services that help make drug R&D more efficient." When the COVID-19 pandemic emerged as a global threat in early 2020, the company decided to employ its modeling expertise in "building a clearer understanding of the public-health risks" associated with the policies being implemented by the CDC and White House, and international health agencies in general.*

The interview was edited for clarity, with many of the scientific terms defined to provide readers insight into the issues at play. Numerous links to papers and studies have also been embedded into the text for those interested in reading further. This interview builds upon prior discussions we held with Dr. Chakravarty in 2022 and 2023.

Benjamin Mateus (BM): It was exactly five years ago when the medical community in Wuhan began to recognize that the patients coming in with respiratory illnesses were infected with a novel SARS-like virus.

Fast-forward to today, and COVID-19 is both ubiquitous in our day-to-day conversations and still very prevalent as a respiratory pathogen in the global community. Close to 30 million people have died due to the pandemic, over 410 million people are now living with Long COVID globally, and one can assume that the majority of the world's population has been infected with COVID on average at least three times. Are there any initial reflections you would like to share on the five-year anniversary of the start of the COVID-19 pandemic?

Arijit Chakravarty (AC): Yes. This is what failure looks like. We are looking at it. No one ever said when the concept of public health emerged in the 19th century, "We really need an organization that is committed to serving as the doula for every newly emergent pathogen that pops out of the wild." The idea that emergent pathogens need to be shepherded into endemicity, this has never been in any public health mission statement.

What we have done is take something that should never have established itself in human communities in the first place and have built a public health consensus around the concept of repeated mass infection.

So, yes, this is what failure looks like. And that sort of normalization of infectious disease is something that we are facing the consequences of now, societally, because those attitudes have crept into other aspects of our society as well. This idea that vaccines are bad, and infections are good. Conflating the idea of coexistence with nature with coexistence with pathogens is a dangerous mess—it will take years to undo this. Honestly, we haven't had attitudes like this about infections since before biblical times.

There really is no historical precedent for this. No society in the world ever said, "Oh, you're infected? Let's let it spread." This whole concept of pox parties being a thing is ludicrous. But that's exactly where we are today. Quarantines used to happen in the 14th century with plague. This uncritical acceptance of infectious disease as a sort of lord and savior is brand new.

And it couldn't happen at a worse time. We're now extremely interconnected. There are more people on the planet than ever before, and diseases can spread rapidly. And the only people that you can really lay this at the door of is public health. Where public health should have been out there saying, "These are the risks of getting COVID. These are the repeated risks of COVID," for which the science is extremely unambiguous. (There are tens of thousands of papers on these topics).

Instead, Public Health was saying, "Masks are the scarlet letter of the pandemic," in the words of former CDC Director Rochelle Walensky. Or "If you have been vaccinated, the pandemic is over for you," which is what Biden said. Trump and his people based their playbook on the phrase , "The cure cannot be worse than the disease." I'm using the US as an example, but you can do the same thing with other countries like Britain, Canada or pretty much any other country in the world. And every single time both public health and politicians have served as cheerleaders for an infectious disease that has clear-cut long-term consequences. None of this was necessary.

BM: You raised a very important point. If you just open a public health textbook, any history book or a novel that was set in the Victorian period, in the 19th century, much of the discussions or descriptions centered on issues of the various diseases that were killing people and, in particular, children. You read the novels of Charlotte Brontë, Charles Dickens or even the playwright Anton Chekhov, death from pathogens is central to their stories.

Although fecundity rates—the number of children birthed—were very high among women, maybe less than half of these children, in the best case, made it to adulthood. The implementation of public health was a watershed period in human history. The social longevity and well-being were rapid and palpable. It was as if a terrifying period had passed because of the public health measures that were being implemented. People living in that period understood it well. They weren't blind to these matters.

AC: When you walk through any cemetery, there's a children's section—any cemetery of a certain age and you can walk through the children's gravestones there. My grandmother was one of 12 children, she was born in the 1920s. India went through a series of bad outbreaks of

infectious disease at the time, plague, the 1918 influenza—she was the only one in a brood of 12 siblings who survived.

At the end of the day the thing that we all must accept is, even if COVID doesn't seem like a crisis now, things could still go sideways very quickly.

With COVID, there are three risks that remain on the table. The first risk is that you have a variant that comes through that has much higher immune evasion. As we pointed out in a preprint of ours, such a variant could very quickly infect a very large number of people—it would be both more transmissible and more deadly.

The second risk is that COVID eventually weakens people's immune systems repeatedly through repeated infections. Everybody gets it once or twice a year and they are much more likely to end up with other health crises.

The third risk is that the virus faces no intrinsic penalty for becoming deadlier. We've shown in a paper of ours that the virus could theoretically kill everybody it infects and still do just fine for transmission. So intrinsic virulence increasing is also very much still on the table.

Meanwhile, you have all this wishful thinking that viruses always evolve to become milder (they do not). That immunity is building up in the population (it is not). Or that somehow pretending like the whole thing is done has made the state of the pandemic better. That's like—you're sitting in your house and watching TV, and you smell something burning and you say, "I'm just going to finish watching my TV show, I'm not going to worry about that burning smell, or the smoke." Maybe you'll be fine. Or maybe you won't.

BM: When you look at the repeated curves of infection, a measure of the number of people who are becoming infected, it dawns on you COVID is not a seasonal virus. What you're seeing during the troughs between peaks is the population immunity waning that makes everyone susceptible again. And then you see another huge spike of infections. And when you do count the number of people that are infected, you see at their peaks 1 or 2 million infections per day sustained for weeks, as with the summer wave. Now the acceleration phase of this peak is a straight wall up. It's jaw-dropping. But more disconcerting is that there is nobody even discussing it.

AC: Agreed. I think it's even worse than that.

First, we've taken a very atavistic or primitive perspective on infectious disease. We are relying on disease and reinfections to manage the acute consequences of infection. The main reason why people aren't dying at the rate they used to isn't because of the vaccines at this point, because most people have minimal protection from the vaccines if they're getting it once a year. Most people aren't even doing that. *(According to the CDC, as of December 14, 2024, only 20 percent of adults in the US have received the 2024–25 COVID-19 vaccine).*

The main reason why people aren't dying from COVID right now is, in my opinion, that they're getting infected on a frequency that's often enough that there's some residual protection from the antibodies left over from the previous infection. And the antibody threshold that you need to prevent severe disease is quite low. So, people are topping up their antibody levels, through repeat infections, at a frequent enough basis that they're not ending up in hospital acutely.

The problem with that strategy is that you're still infected all the time. It has been well-documented that the virus can make its way into pretty much every tissue. These have many long-term consequences that are subtle but have huge implications. First, brain infections have been documented. Cardiac risk has been documented. There is a two-fold elevated cardiac risk shown to persist for at least three years. You can also make a case that SARS-CoV-2 infections are directly carcinogenic. I've put up threads on my social media on this topic, we're also drafting a manuscript on this topic. Others have also made the argument that SARS-CoV-2 is carcinogenic.

Now, separately, cancers were rising before SAR-CoV-2 showed up. In the 2010s, cancer rates were rising among young people. This can distort the signal caused by SARS-CoV-2 infections. If SARS-CoV-2 causes cancers to increase, if it is carcinogenic, it'll take a big increase in that rate of cancer before people acknowledge that SARS-CoV-2 is now a contributing factor. Similarly, heart disease rates were rising anyway and now we have a virus that is causing increased heart attack risk.

And because it will be harder to see the signal for cancer, it means we are kicking the can down the road with all these delayed consequences. And then at the same time, it's quite easy to hide the delayed consequences. And what that means is on the day that they acknowledge that this is what's happening, we've locked in this huge burden of delayed disease that will take years to play out because people have already been infected many times over.

So, this is exactly how not to do it. When I said we are taking a primitive approach to disease, we are managing disease through allowing infections, which had never been done before.

The second thing is you're basically throwing the precautionary principle out the window. That's gone. And on top of that, to make matters worse, the very same people who have taken us down this path are out there taking a victory lap.

There's all this talk about how there was overreaction during the "lockdowns." Go look at Google mobility data. If you can spot the lockdown in that Google mobility data for 2020, your eyes are sharper than mine. Literally the lockdowns they called overreaction looked like a 30 percent decrease in people using public transit for three months. You must squint your eyes to see the drop in the number of people going into restaurants, number of people going into retail stores. You have to squint to see it. And it was literally for only a few months. And now, these legendary lockdowns which somehow happened without any of us noticing them are being blamed for all the deaths and illnesses the virus has caused.

Given this revisionist history, the narrative that's being put on the table is that somehow these people were right all along; that it was absolutely the right thing to allow everybody to get infected repeatedly. When the bill comes due on all this, there will be no accountability because this will take a while to play out and all these people will be gone by then.

This is a difficult virus from a public health perspective, but public health couldn't have handled it worse. Although it remains a solvable problem, the way it was addressed has undermined the ability of public health to do anything useful at this point, given the current leadership and controls over public health as they stand. They are doing nothing except reminding us to wash our hands and not eat raw eggs.

BM: On the topic of carcinogenesis of SARS-CoV-2, can you comment on some highlights you'd like to share from your manuscript before it's published? *(Links: 1, 2, 3 and 4. The issue of cancer and SARS-CoV-2 is emerging as an area of research.)*

AC: The short version is that it's very well documented that SARS-CoV-2 causes DNA double-strand breaks. [*The reader can read this report in the journal Nature on the mechanisms SARS-CoV-2 employs in deregulating cellular machinery and causing DNA damage and the cell's ability to repair these.*] There have been multiple papers that show that it causes unrepaired DNA double-strand breaks. It also inhibits elements of the DNA repair machinery, some of which are oncogenes and some of which are tumor suppressors.

In the old conception of carcinogenesis, there was always emphasis on the role of oncogenes driving cancers. If you will, oncogenes can be viewed as the "accelerator" and tumor suppressor genes as "brakes." There were billions of dollars spent on hundreds of drug discovery and development programs ("precision medicine") across the pharma industry pursuing the oncogene addiction hypothesis. [*See work by I Bernard Weinstein*]. It hasn't really panned out.

There's an alternative paradigm for thinking about what drives cancer, and that is the evolutionary paradigm (which I explained in a recent thread on social media). In this paradigm, the initiating event for cancer is the initiation of genomic instability, due to DNA double-strand breaks. Now ordinarily, if there are DNA double-strand breaks, the cell will arrest replication and either repair that damage, or if irreparable, initiate cell suicide to prevent propagating the errors to the daughter cells. But sometimes, the checkpoints that would have prevented cycling of cells with those breaks continuing to replicate are suppressed.

So now, these errors are not caught and repaired, and if a cell has accumulated enough DNA double-strand breaks, the cell can no longer maintain its complement of chromosomes. So, it becomes what's called chromosomally unstable or genomically unstable. There are other ways to get to genomic instability, but for now, let's just focus on chromosomal instability.

When you have chromosomal instability, when cancer cells divide, they reassort their chromosomes every time. That generates a tremendous amount of diversity. This evolution is what fuels the growth of cancer. There are multiple lines of evidence that show that cancer evolution is somatic clonal evolution. You have these different subclones within a patient that evolve differently. When people have done high-throughput sequencing of these, the genetic status of even different pieces within the same tumor is different. And when you go look at metastatic tumors, these are very different genetically from the primary tumor. To describe all this, it's as if a bomb hit the genome, basically. That's not consistent with just one dysregulated oncogene that is driving the cancer. Genes don't drive evolution. Genes are acted upon by evolution.

BM: And how does SARS-CoV-2 impact that?

AC: It causes DNA double-strand breaks and suppresses DNA damage checkpoints.

The DNA double-strand break is the initiating event. Downstream of that you have the suppression of checkpoint signaling. In the process you get micronuclei, which are little fragments of DNA hanging out in nuclei of cells in interphase [*of the cell cycle: a cell spends most of its time in what is called interphase, and during this time it grows, replicates its chromosomes, and prepares for cell division*]. Guess what happens with SARS-CoV-2? We see micronuclei formation.

You might think, "Okay, this is happening, but it can't be oncogenic because it's not transforming any cells. So, if this happens in a quiescent cell [*a cellular state in which a cell remains out of the cell cycle but retains the capacity to divide*], who cares?" Here's the thing. SARS-CoV-2 doesn't just infect cells that are not actively cycling [*differentiated cells in mature tissues*]. It's very well documented to infect many different cell types, including cell types that are proliferating.

If you look in the liver or the gut where cells are constantly dividing and reproducing, there are also SARS-CoV-2 infections. In the crypts of the gut, you have cells dividing repeatedly. People have directly documented that SARS-CoV-2 infects those cells. And they've directly documented that it causes cell death.

Putting all this together, you can make an obvious inference that if those cells keep getting infected and they keep dying and new cells come in, there's going to be some subset of those cells that accumulate DNA double-strand breaks, and that are capable of cycling. That would be both necessary and sufficient to cause, for example, colorectal cancer. Now you're seeing an increase in colorectal cancer among the young already. The problem is that we saw that increase before COVID showed up. So, it's very difficult to ascribe that increase specifically to SARS-CoV-2 infections. It's like the worst of both worlds, frankly.

You can make the case inferentially from first principles logic that this is what would happen, and, indeed, it does happen. But if you try to show it epidemiologically, it's very difficult because you're dealing with the obscuring factor of a prior increase, which makes the point that when you have something that you can build a plausible case for—SARS-CoV-2 has the potential of driving carcinogenesis—waiting for enough epidemiological data to make that decision could be a huge mistake.

But that's the route we're on because every article indicating that SARS-CoV-2 can cause cancer also adds, "But it's too early to tell." But by the time we determine it's not too early to tell, everybody will have been infected 20 times. SARS-CoV-2 causes the same genetic changes as every other virus known to cause cancer. [*The idea that viruses can cause or lead to cancers is not new. Viruses like the Epstein-Barr virus, hepatitis B and hepatitis C viruses, HIV and human papillomavirus are well-known pathogens associated with malignancies*.]

BM: This discussion takes us back to the false conception that there is an "immunity debt" that needs to be paid that justifies the concept of mass infection in perpetuity. This notion has been spread in particular since 2022, when hospitals in the US and globally began to get slammed with RSV, flu and other patients, especially children, with limited lockdowns and public health measures from 2020 supposedly to blame. Yet, no one discusses the impact of immune dysregulation caused by prior SARS-CoV-2 infections for the likelihood of acquiring more severe cases of the flu or RSV. Can you speak to that?

AC: I'm not sure who exactly it was—one of those "infectophile" physicians—who went out in public a while back and said "immunity debt" is going to last for a generation. Hats off to them. It's clever, right? Because they know what's happening and they're already clearing out that wiggle room for themselves for a generation. Presumably by that time, they will have retired and be laughing all the way to the bank. If you can find a mechanism that would explain why if you don't go to your local bar for six months it could cause immune dysfunction for the rest of your life I'd love to hear it. I haven't read that paper yet.

There are no papers on immunity debt from before the pandemic started. The concept started in 2021 and has been promoted by people like Alasdair Munro, who is a clinical research fellow in pediatric infectious diseases in the UK who has made a name for himself publishing this kind of stuff. There's always going to be scientists who are willing to corrupt themselves by making statements that everybody else can point to when they have vested interests.

The way I look at it is that when we look at the immunity debt hypothesis, you should be able to show that there was this amount of displaced infection during the lockdown period. First, find the lockdown period and then show me how many cases were reduced. And then if what you're saying is true, then the following year, there should have been an increase in infections.

So, as happens, you can actually see this effect with certain diseases. I think flu, for example, was one disease that showed a distinct decrease when people were wearing masks. The following year, you had elevated rates of flu. But if you displaced a million infections during a period when people were getting infected less often, and then in the following years, you had 10 million infections, explain the mechanism. How is that happening? And those are the numbers.

And the point is that we are seeing more and more infections of various types. There are published studies that show that the total number of infections, different kinds of outbreaks, infectious disease outbreaks, have risen dramatically in recent years. And those papers, written by the likes of Munro and his ilk, will then quickly ascribe it to immunity debt. Again, because there are one or two of those "fact-free" papers out there that lie at the bottom of this sort of rotten pseudo-scientific edifice that people point to and say this is immunity debt. The actual mechanistic pieces of immunity debt, however, these people are not working on elucidating.

BM: There are papers that show that children with prior COVID infections had higher rates of and more severe RSV infections compared to children without a prior COVID infection.

AC: That's another thing that they can't explain in their immunity debt

hypothesis. That paper showed both the risk and severity of RSV go up after a prior COVID infection. So, explain to me how not having RSV in the previous year can increase your risk of being hospitalized this year. That's not a thing, right?

BM: Rather than enhancing our public health posture and scientific understanding of diseases, there's been the opposite effect through growing vaccine hesitancy, mistrust of science, cavalier attitudes towards infections and diseases and the embrace of personalized perspectives on communicable diseases. Meanwhile, every day we grow closer to seeing a bird flu pandemic become a reality. What are your thoughts on this?

AC: I'll take one step back. I see the bird flu situation a little bit differently. I'm 95 percent of the way with you on this issue and I think the reporting on the WSWS has been excellent.

If you look at the 1918 influenza pandemic, the 1918 influenza virus has a segmented genome that can readily mix and match with other flu viruses. There were a couple of critical mutations that got picked up in that flu virus. People have done phylogeny, pulling bodies out of the permafrost and then sequencing the influenza genome from the victims of the 1918 pandemic. So, they were able to reconstruct the lineage.

What they found was that the emergence of that virus happened in stages. It most likely circulated for a period jumping from birds to pigs somewhere at the turn of the 20th century. It probably circulated in pigs for six to 12 years, and then at some point around 1918, literally months before the pandemic, the different pieces, the different segments of the genome got put together.

There are only a handful of mutations, I think two or three mutations, that gave the 1918 influenza its killing power, its pandemic power. But those mutations came together in pieces through the previous decade. It was really bad news that it was circulating in pigs, but very different from COVID. Influenza evolves very slowly. COVID, on the other hand, evolves rapidly and is very tolerant to mutations.

My point is that I think that H5N1 in dairy herds is really bad news. I think it's unconscionable that they allowed this to happen, because they are essentially incubating a pandemic potential virus at scale, in multiple different live subspecies. However, I couldn't predict for you when that pandemic would explode. It could explode tomorrow. It could explode six or 12 years from now. The fact that we are pretending like this is not a thing to me is just jaw-dropping.

There are whole plans around influenza pandemics. Governments have spent millions of dollars on preparing for the next influenza pandemic plans. What I never realized was that once they made these plans, they said, "Problem solved! We know what to do. We're not going to do it, but we made the plan."

I find that remarkable. The surveillance situation is just beyond bizarre. The idea that they are allowing the virus to spread among cattle, poultry and humans and see what will happen is terrifying.

If you look at what happened in 1918 at Camp Funston (today Fort Riley, Kansas) when the epidemic first broke out, the body count racked up fast. In two weeks, all hell had broken loose. And that was in an era when it would take people two or more weeks to get from one end of the globe to the other. If something like that happens now, out of a farm somewhere in Iowa or Kansas again, it will be a week or so before half the world is severely infected with this thing.

What I find remarkable is not that this pandemic is imminent. It is that they have created conditions that make a pandemic not only plausible, but likely. And then they have also gutted the public health infrastructure such that their plan on paper is not worth the ink they used. The whole thing is just a joke—I think we are worse off today than we were in 1918.

BM: You said earlier that although the COVID virus is a difficult virus to deal with, the possibility continues to exist to address it. Can you elaborate on this?

AC: It is primarily difficult to deal with because it has a lot of characteristics that make it tricky. One, it kills slowly. Two, it has a low infection fatality rate. Three, it is highly contagious. And four, immunity wanes very quickly.

All of that said, essentially the first obstacle we must deal with is the idea of pandemic denialism. We are like lemmings at this point. There is no real appreciation at the public level for the scale of threat we are facing.

The first thing that public health would need to do, long before we get to nasal vaccines, is to stop the lying. We need to tell people why it's bad to get COVID repeatedly. Tell people why COVID can shorten one's lifespan. I think most people who are alive today will face the reality that COVID is a contributing factor to their death. Do people know this?

You have a 65-fold increased risk of a heart attack on day zero of COVID if you are vaccinated (the number is approximately double that if you're not). It is very likely COVID can contribute to cancer. COVID decreases your overall immune responsiveness. It's very likely that COVID causes 50 other things. You can build these cases from literature. In fact, there are so many papers on COVID that people can't keep ahead of it, there are literally hundreds of thousands of papers on this topic. But I've never seen such a wide disconnect between what the public thinks and what science says.

COVID is not inconsequential, and our public health leadership has been complicit, actively participated in making people believe it's just another run-of-the-mill respiratory virus. And that is problematic too. If people really understood the science behind all this, they would have a very different attitude.

For example, I wear a mask when I travel to India. When I wear a mask and people ask me, why do you wear a mask? I say, "COVID." And everyone says, "Is that still a thing?" And then people act somewhat worried because in India, when COVID hit the cities, you could smell the funeral pyres burning. Everybody knows that COVID is a deadly disease in India because we Hindus dispose of our dead in a way that's not that discreet. In the West, the bodies go into the ground, so it's much easier to literally cover it up. So, people to this day believe that nothing really happened, even though a million and more have died.

So, the lying must stop is the first point.

The second point is if you want to control this virus, you have to deal with the threat that it represents. And the threat that it represents principally is the fact that it is evolving extremely rapidly. That rapid evolution creates a massive tail risk which is a mass death event very quickly and with very little warning. That risk, the possibility of such a turn of events, must be addressed even if it makes people uncomfortable. Otherwise, it will be difficult to mitigate COVID. The rapid viral evolution of COVID creates a massive tail risk for us, not only as individuals, but as a species.

[*Tail risk is a financial term employed to assess a risk of an asset or portfolio. These investors are generally more concerned about unexpected losses rather than gains. The term is sometimes defined less strictly as merely the risk or probability of a rare but high-consequence negative event.*]

Nassim Nicholas Taleb, the author of the Black Swan paper, wrote a paper in early 2020 stating that pandemics are "fat tail" risk events, meaning that the death counts from pandemics do not taper off the way you would expect in a "normal" distribution. Historical pandemics have had very fat tails. But if you keep playing roulette—allowing repeated waves of COVID infections to occur—the house will eventually win. I mean that with repeated waves of COVID it is near certain that at some point we are going to have massive unanticipated consequences with this non-public health strategy.

Not only are we not taming the virus, but by playing roulette repeatedly, we will eventually hit that "outlier event." But then they will say no one could have predicted it. This whole idea that somehow repeated waves of

infection will make things better flies in the face of any rational science. The virus is not incentivized to become milder. And each time we afford the virus the opportunity to hit the jackpot, a combination of mutations that evade existing immunity with a high virulence, it could be catastrophic. Whether that takes two, four or 12 years, I can't tell you. But I can tell you that this is not the way to solve this problem.

BM: How do we solve the problem?

AC: First, we should talk about what the problem is. The first problem is that we are leaving a threat on the table that is completely undealt with, which is the risk of rapid evolution and a catastrophic event. The other problem that we have is that, by repeatedly reinfecting people with the virus, we don't know all the long-term consequences (although the emerging evidence suggests that the long-term consequences will not be good). These are the risks of repeated exposure to the pathogen, and we need to be honest with people on these.

The good thing about COVID is that it has a lot of evolutionary vulnerabilities. So, if you really want to slow down the evolution of SARS-CoV-2, and if you set that as the public health objective, it's quite doable.

One vulnerability it has is a narrow bottleneck when it goes from one person to another. It only takes about 10 viral particles, which means it finds it very difficult to optimize because it's going from one person to the other. Although it exists within your body as a very wide range of viral particles known as quasispecies, it still is a very small sample of that that goes from one patient to the next. So, despite a wide genetic variability, only a handful go to the next person. That's not efficient in promoting genetic variability.

The main way we are seeing large jumps in the evolution of these viruses is through a process called punctuated equilibrium [*a term used in evolutionary biology*]. This occurs in people with long-term infections such as those who are immunocompromised and the virus develops a chronic active state in the person. Long-term infections are much more efficient at generating better viral particles. And when these particles spread onwards from long-term infections they create the risk of a punctuated equilibrium event.

Punctuated equilibrium events, it turns out, are just really bad news from a public health perspective. The 1918 influenza pandemic was started by the product of a punctuated equilibrium event. The Black Death, the argument has been made, was caused by a punctuated equilibrium event. In other words, a large evolutionary jump can really create a lot of problems for human populations.

So, what you want to do is to stop those large evolutionary jumps for SARS-CoV-2. And the one obvious way you can do it is limiting onward spread and developing combination treatments *specifically* for long-term infections. This should have been done years ago. It's not too late to do it now. Basically, we should identify people with long-term infections that are capable of infecting others. We should find ways to limit spread from them, and we should give them treatments that are specifically designed to bring the viral load down.

But you don't want to just give Paxlovid to everyone with a long-term infection because they're already harboring highly mutant forms of the virus. So that's a great way to wreck your frontline treatment for the general population. Instead, you want combination treatments that are reserved for use with long-term infections.

Beyond that, you want to use a multipronged approach to reduce global viral load. Having more viruses around, at a global level, is a terrible idea because you've created a situation where there are probably more particles of this virus than of any other pathogen that humans have. On any given month there are hundreds of millions of people infected with trillions of viral particles. That is a recipe for disaster.

If you really want to bring the global viral load down, of course, then the most obvious way is to improve indoor air quality. It's been well demonstrated by a lot of people that indoor air quality alone would get rid of a large chunk of the total viral load. It doesn't have to get rid of spread as long as it brings the total viral load down. You can also do this by using other kinds of engineering controls such as monitoring air quality in a room. Much of that technology exists today. There are also far-UVC lamps that can be employed. Deploying HEPA filters, you could probably up the indoor air quality in every building in the US for the cost of an aircraft carrier. Sell a couple of aircraft carriers and upgrade indoor air quality. It's expensive, but it's on that scale that it's doable.

We spent 5 trillion dollars during the pandemic, but we didn't fund research. Thirty billion went to the vaccines, Operation Warp Speed, which as a fraction of the 5 trillion is less than 70 cents for every $100. The rest of the COVID research for new therapeutics got, I think, around $2 billion. Less than the beta amyloid hypothesis for Alzheimer's research in that year.

We still haven't put in much into the whole problem of antivirals and better vaccines. When you look at it from that piece of it, there's room to improve. Vaccines against non-spike proteins would have been a much better way to go about it. Having multiple viral proteins being targeted with antivirals, even as you're improving vaccines, would be great.

This whole idea of nasal vaccines is a great idea and concept, but it's technically very challenging. And when we put all our hopes on a single technological advance, we fall into the same trap. We did this five years ago. We haven't learned the lesson. We should not have put all our eggs into the vaccine basket, but indeed we did, and here's where we are. You could say maybe a nasal vaccine will fix this. I'll bet you that it won't, if you use it alone. Any intervention, if you rely on it alone, will fail because you're up against evolution. So, a multipronged approach is what you need.

I think if COVID nasal vaccines show up, that would be great. But the idea that you can get an evolution-proof vaccine for coronaviruses, I find amusing. There's no such thing as evolution-proofing anything.

Sotrovimab (brand name Xevudy) is a human neutralizing monoclonal antibody that showed activity against COVID. It was found by looking for sequences in the beta coronavirus family that were less prone to evolution. The reason you don't hear about Sotrovimab anymore is because the FDA pulled the emergency use authorization after three months when they found it had no efficacy against Omicron. So much for your evolution-proofing.

We showed in a paper in 2021 that the virus can defeat any individual monoclonal antibody with just the standing genetic variation that was present in the population in 2020. Five years later, people still haven't digested the lessons on that paper, which was that you shouldn't try this at home, friends. This is not the way to go about dealing with a virus that's rapidly evolving. The whole evolution for vaccine ideas is a dead-end. But if you went in with nasal vaccines that prevented transmission, that could be useful.

We have a manuscript in the works and we've pointed it out previously as others have, you could do a lot better with scheduling the existing vaccines you have. Our paper shows that if you dose more frequently, you probably end up with higher concentrations of neutralizing antibodies, which would make it more difficult to get infected. Our prediction was that three or four doses a year could help prevent infections. But those studies on different vaccine schedules are not being done.

I think the most important point is you want to maximize the diversity of neutralizing antibodies. What we did with Operation Warp Speed was the single stupidest thing we could have ever done, which is we concentrated all our efforts on targeting a single spike protein which we then targeted with antibodies. But this was the one thing that the virus was designed to do, which was to evade such antibodies. I use the term "designed" loosely. But basically, we proved through our vaccine construction targeting the spike protein that the virus is evolutionarily optimized to circumnavigate such threats like it was nothing. And we predicted this in

the fall of 2020. We predicted that the vaccines alone would not be enough to bring the pandemic to an end, and we predicted that the virus would rapidly evolve to defeat antibodies, and it played out that way.

If you want to avoid making that same mistake again, don't put all your eggs in the neutralizing antibody vaccine basket or in the nasal vaccine basket. Don't put all your eggs in the evolution-proof basket. It isn't going to work. The story's going to end the same way as it did last time.

But if you come in with a multipronged strategy where you limited onward spread from long-term infections, you develop combination therapies for long-term infections, you use the multipronged approach to reduce the viral load, including deploying things like HEPA filters and far-UVC and monitoring viral load in public spaces, now you have a fighting shot. If you then use a variety of different vaccines to really maximize the diversity of neutralizing antibodies at a population level, the odds of slowing viral evolution down to a crawl start looking good.

The bottom line is that if public health had stopped lying years ago and had been honest about the costs, and if public health had realized what the correct approach is, which is to slow evolution down, then we would have been in a situation today where public health was treating COVID as a disease that needs to be suppressed.

The whole canard from day one was that we would never eliminate or eradicate it, so, let's let it spread as widely as possible. "Learn to live with it," for other diseases doesn't mean the same thing as we have applied to COVID. When we say we must learn to live with leprosy, we don't mean let's make sure everybody has leprosy. When we say we must learn to live with malaria, we don't mean let's make sure everyone gets malaria as often as possible, let's keep mosquitoes lurking in our tanks outside our house. No one says you must learn to live with tuberculosis. Let's let it spread as much as possible and see how that goes.

No, we suppress those diseases every step along the way. We suppress dengue. We suppress tuberculosis.

This whole idea that learning to live with the disease means permitting and encouraging its rampant spread and rapid evolution is just so many levels of stupidity that I don't have a word for it.

BM: I'd like to know your thoughts on Trump and RFK Jr., his choice for secretary of health? RFK Jr. has been at the head of vaccine disinformation and anti-public health policies. They are calling for ending any cooperation with the World Health Organization. These will have immense consequences for public health globally. These are political questions, but often I hear scientists do not want to engage in political questions and feel uncomfortable about it. Can we avoid the political implications?

AC: Look, it's not that I don't want to get political. It's that if I was going to get political, I don't know who to hold up as an example. There's not a government in the world that has handled this correctly. There's not a party in this world that's handled it correctly. It's all different flavors of stupid.

Pick your poison.

The Democrats went out of their way to normalize mass infection. They went out of their way to lie about the vaccines and say, "If you're vaccinated, the pandemic was over." That was completely unnecessary. It was completely at odds with science. Then you have Trump in the first Trump administration saying, "Why don't you drink some bleach?"

It would be a comedy if the consequences weren't so grave. Frankly, wherever you go it's like this. You look at Canada's Bonnie Henry (Canadian epidemiologist and physician) in British Columbia. On day one she insisted that the kids wouldn't get infected. Then she went and published a paper, put her own name on it, bragging about how herd immunity has been achieved because 90 percent of Canadian kids have been infected.

In the UK you had the hearings on the public health response by the UK government. They noted that the government failed to act quickly. There was no clear policy approach, and they even abandoned contact tracing in mid-March of 2020. They even said that masks don't help stop the spread and the virus wasn't airborne. It's a disgrace.

Politicians worldwide have decided that they can brazen out their way through this. And the reason for this is they've been advised by a certain set of scientists, a relatively small number of scientists, who have essentially sold out.

There are tens of thousands of papers, if not hundreds of thousands of papers, on the risks of COVID. You could literally find thousands of scientists who would be willing to go up in front of the House of Representatives and testify that getting COVID repeatedly is bad for you.

Where are those scientists? Nobody's listening to them.

They're listening to the scientists who whisper in their ears and say that everything will be okay. Ryan Gregory and I wrote a Substack blog post a while back called Calm Mongering where we talk about this—that people have weaponized the logic of science in the service of propaganda by saying, "that's just a hypothesis." As soon as you bring up a risk, these "experts" shut down the conversation about the risk by saying we're not sure that'll happen. But in fact, that's an inversion of the precautionary principle. And it's a lot of the tactics that were used by the merchants of doubt during the tobacco era. The merchants of doubt were a subset of a very small number of corrupt, well-connected and well-funded scientists who went out of their way to make public statements that were at odds with the body of literature that was coming out on lung cancer and tobacco.

And we are seeing the exact same thing again. Big tobacco sponsored a bunch of corrupt scientists to create a counter-narrative to reality. This time around, who's playing the role of big tobacco? It's the politicians and governments. But the exact same thing is playing out. That nexus between this group of corrupt scientists and politicians who are actively funding their work is a global phenomenon. Unfortunately, I hate to say this, but it's going to take reality breaking through to solve this. They've been very effective at convincing people that this is not a problem you need to worry about.

On top of that, they've undermined any trust in public health. You've driven it back into the 18th century. And all of this is being packaged as a win. So, I don't disagree with you that the Trump administration will make things worse. But again, there's only so much you can do to defy gravity. If you jump out a window and you insist that gravity is not going to apply to you, you are facing a "Wile E. Coyote" situation. And we are at that "Wile E. Coyote" point where governments worldwide have driven us off the cliff and it's just a matter of time before gravity kicks in.

BM: I would take issue with one of your comments. The Socialist Equality Party and the *World Socialist Web Site* have, from the beginning, sounded the alarm and called for a unified scientific perspective in response to the COVID-19 pandemic. We called for an eradication/elimination strategy early on. I would argue that at least the Trotskyists have proven their mettle and put their pen on the right side of history and science.

AC: I'm a big fan of your work and what you guys have done on COVID. And I would say I'm very aligned with what you guys have said on this subject.

One of the things I would say to you is it's not so much eradication or elimination as it is just suppression. Suppressing disease is something we pay these people to do, and they do it for every other disease.

If they told us not to worry about tuberculosis because we can never eradicate it and let it spread, we would immediately ask them what are they doing with the money we give them. They should just do their damn job and suppress this disease like other diseases. And as I pointed out, there's five or six things they could be doing tomorrow, none of which are hideously expensive, that would over time lead to suppression.

If you could get to the point where the disease is suppressed, where you

have local outbreaks here and there, where you don't have people getting it twice a year, you're in a much better situation.

I do appreciate what you guys do in this respect. And I think it's thoughtful, science-driven coverage. But again, the only thing I would say, the only place where I would see it a little bit differently, is that suppression is a goal in and of itself. There's no disease in the world that we don't suppress.

BM: Any final words, Arijit, as we conclude this fifth year of the pandemic?

AC: I hope we're not doing this again in five years.

BM: I'll take that as your final word!

AC: I think at the end of the day, it remains a solvable problem. It's disgraceful the way that this has unfolded. And I think that if you're out there taking COVID seriously, and if you're out there still trying to avoid repeated infections, you're still doing the right thing. It is still possible to avoid being infected and a worthwhile goal.