COVID-19 UPDATE—The good, the bad, the confusing: Latest developments in the treatment pipeline for the novel coronavirus

In a previous newsletter article, I outlined the most plausible *natural*preventive and treatment strategies for coronavirus. Herein, I'll share some of the most promising avenues utilizing repurposing of currently-available drugs, fast-tracking of newly-developed agents, or ingenious

deployment of traditional strategies like convalescent serum and vaccines.

All the buzz is about **hydroxychloroquine** (brand name Plaquenil) which has shown promise when combined with the antibiotic azithromycin (brand name Zithromax or Z-pak). Hydroxychloroquine is an anti-malarial, and azithromycin is an anti-bacterial, so how does that make sense when we're dealing with a virus?

It appears that there may be ancillary effects of these drugs, not that they're directly killing the virus. They may block "docking" of the coronavirus on cell surfaces, or else they may reduce the inflammation that causes patients' lungs to fill with fluid and their organs to fail. It's still unclear precisely how that might work.

The craze for this combo was promoted by preliminary reports from French doctors in Marseille who saw dramatic turnarounds in their sick patients when administered this combo. Unfortunately, rational investigation of these drugs' potential has been distorted by politicization after President Trump's seeming endorsement of giving them a try. He's been lambasted for prematurely promoting an unproven therapy with potential harmful side effects.

The jury on Plaquenil for COVID-19 is still out. I've been tracking the early research, and even attempting to obtain the combo for some of my sicker patients. One recovered rapidly after beginning the double-barreled treatment—but he may already have been on the mend by the time we secured the hard-to-source medication.

In fact, health professionals are taking advantage of their prescribing privileges by rushing to hoard supplies of the scarce drugs for themselves and their families. Out of concern for sick patients and health professionals exposed to the virus on the front lines, I've decided *not* to do that for

myself personally nor for my family members, and I discourage well persons from stockpiling. I have a long memory of recent times of previous stampedes (post 9-11 when people rushed to obtain Cipro vs. anthrax and in the 2000s when folks demanded near-useless Tamiflu vs. H1N1 flu).

Some states are restricting private prescribing of Plaquenil and diverting supplies to hospitals where front-line doctors seem to be liberally prescribing it. Some of my colleagues report it's not helpful, especially in critically ill patients; but other accounts are more encouraging.

It's worth noting that Plaquenil and its predecessor anti-malarial chloroquine (not to be confused with the ingredient that's used to clean fish tanks!) are not harmless panaceas: long-term use of hydroxychloroquine requires careful surveillance for eye changes, but short-term use should be OK. More concerning is that both Plaquenil and Zithromax can cause QT prolongation on ECGs—a potential harbinger of deadly arrhythmias. Some of the sickest hospitalized patients with COVID-19 have heart problems, and are hence vulnerable to these side effects, but at least they're being monitored in intensive care. I worry about elderly or heart disease patients dosing themselves with high doses of Plaquenil while unsupervised at home.

At any rate, clinical trials are underway around the world, and we should learn definitively this month if the hydroxychloroquine/azithromycin frenzy is justified, or whether we're simply grasping at straws.

Antihypertensive drug controversy: Which is it? **ACE inhibitors or ARB** drugs are other *good* or *bad* for COVID-19, depending on who you're listening to. This is based on the recognition that the virus uses angiotensin converting enzyme (ACE2) pathways to do its dirty work. This has prompted some "viral" warnings that people consider stopping their blood pressure drugs (only certain types)—which is unwarranted, unsubstantiated, and

dangerous for people who depend on these drugs for blood pressure control.

Conversely, others have said that certain BP drugs might actually *help*. Losartan (brand name Cozaar), a popular angiotensin receptor blocker, has actually been proposed as a treatment for COVID-19 and is under investigation at the University of Minnesota. The researchers propose "that losartan can reduce fatality rates in those who have been hospitalized and reduce hospitalization rates by up to 50 percent. Losartan helps reduce inflammation in the lungs, which is the main cause of death from COVID-19 when that inflammation leads to acute respiratory distress syndrome, or ARDS."

Similarly, confusion has arisen over the safety and desirability of using **ibuprofen** for treating fever and body aches in COVID-19. A hasty warning was issued early in the epidemic by authorities in France, which was echoed by many, then contravened by the World Health Organization. But the concern went viral nonetheless.

The European Medication Agency (EMA)—the equivalent of the US FDA—issued a statement exonerating NSAIDs: "There is currently no scientific evidence establishing a link between ibuprofen and worsening of COVID-19".

But I say to patients and my audience, give your body's defense systems a chance to fight the virus with a modest fever; so-called "heat shock proteins" are part of the body's healthy immune response to pathogens. Fever therapy has been a part of medicine from time immemorial. Sure, if your temperature exceeds 102, feel free to pop an occasional Tylenol or Advil to ease your discomfort, but don't overdo it. Those medicines are to make you feel more comfortable, won't help you fight the virus, and they have side effects.

Antivirals have proven effective against HIV, and, to a lesser

extent, against other viruses like influenza and Ebola. Therefore, it's plausible we trial them vs. Coronavirus. But a couple of protease inhibitor cocktails have already struck out; **Remdesivir**, a Gilead Pharmaceuticals drug originally targeted for Ebola, looks more promising; it has been repurposed and is undergoing extensive clinical trials for COVID-19.

One of the most exciting alternatives for treating Coronavirus is actually based on a concept pioneered in the 19th Century: **convalescent serum.** Before the advent of antibiotics, it was the only game in town; studies conducted during the Spanish influenza pandemic of 1918 to 1920 suggested that the use of convalescent serum from recovered individuals might be effective.

Calls are already out for volunteers with confirmed COVID-19 to donate plasma after a suitable quarantine period has elapsed. New rapid and sensitive blood tests that can detect antibodies may soon help us discern who's no longer infectious, and who possesses the critical immunoglobulins that can boost vulnerable individuals' defenses. Ongoing trials will soon tell us if it works, and if it's safe.

Vaccines are another route for addressing the pandemic—not in the near term because vaccines take a long time to develop and test for safety and efficacy, but against the possibility that we'll see a resurgence of Coronavirus after the lockdown is lifted in the fall and winter. At least eight different vaccines are under investigation and may be fast-tracked.

For the sake of argument, let's momentarily put aside the current heated controversy over vaccine safety. It's one thing to propose mandatory universal vaccines for conditions that are rare or relatively mild; Coronavirus is a killer, and its paralyzed life as we know it, so extraordinary circumstances may prompt us to embrace therapies we'd ordinarily be reluctant to accept.

But I have some real concerns about vaccines for Coronavirus, and many respected voices in the scientific community—Dr. Anthony Fauci included—share them. Ill-conceived universal vaccine efforts in response to a new pathogen have in the past caused more harm than good—witness the much-critiqued over-reaction to the Swine Flu during the Ford Administration which caused a rash of Guillain Barre cases, and LYMErix vaccine for Lyme disease that could trigger crippling arthritis.

But most concerning is that a Coronavirus vaccine could confer modest but incomplete protection against the virus, and that when you contract COVID-19, you could experience exaggerated symptoms due to "immune system priming". This phenomenon has already been demonstrated with the Dengue Virus vaccine, and a 2012 studydocumented it with a SARS vaccine—which was targeted against the antecedent of today's Coronavirus.

I'm not saying that an eventual vaccine might not be safe and effective, but I'd be pretty reluctant to recommend it to my patients and family members without thorough testing and a proven track record which may take many months or even years to establish.

I'll keep you updated on new developments with special editions of my newsletter and timely podcasts as we all hunker down to face the COVID-19 pandemic. Be safe, practice social distancing, and wash your hands!

***The preceding information is not intended as medical treatment**, but rather a review of the current science. This information is not comprehensive and will be updated as new information emerges in the literature. Consult your physician for advice on the latest potential treatments that must be tailored to your unique medical circumstances.*