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Trust in the Time of COVID-19

In mid-March, a longstanding patient called my office, asking for hydroxychloroquine to ward off COVID-19. His call came on the heels of a press conference touting the miracle of this wonder drug. I had managed his stable ischemic cardiomyopathy for over a decade and in that time, he had called me only once, from Europe, when hospitalized with shortness of breath. A continent away, I could not titrate diuretic therapy or optimize afterload reduction. But I called him every day because he told me that my familiar voice on the phone was comfort enough. When he returned to Los Angeles, he hugged me tight, tears in his eyes, and I could feel the trust between us growing stronger.

After the presidential endorsement of hydroxychloroquine, I had braced myself for a flood of patient calls. Though I am a cardiologist, I had prepared a response based on evaluation of peer-reviewed publications, scientific statements, and internet anecdotes. I could have punted to his internist because that would have been easier than denying his request, but I did not. He trusted me, and I owed him an explanation for why I would not prescribe prophylactic hydroxychloroquine.

I began with theory: *in vitro*, hydroxychloroquine inhibits growth of SARS-CoV-2. I contrasted the theory with practice: there was no evidence that hydroxychloroquine prevented COVID-19, reduced the severity of illness, or increased survival. I outlined the potential side effects and drug interactions. Finally, I appealed to his ethics: if I were to prescribe unnecessary hydroxychloroquine for him, then the supply might be compromised for patients with serious inflammatory conditions such as lupus or rheumatoid arthritis.

I expected chagrin; I was not prepared for his anger. He told me that “everyone” said hydroxychloroquine worked. How could I withhold this medical miracle? Since I would not give him hydroxychloroquine, he would investigate other sources.

The rest of the day passed in a blur of telephone and video visits interspersed with web conferences on surge

planning, yet I could not stop thinking about our conversation that had gone so wrong. For ten years, he had arrived at his bi-annual appointments on time and never questioned my advice. When stranded in Europe, I was the physician he trusted enough to call. So what had changed?

That afternoon, my mind raced as I drove home through the eerily deserted streets of Los Angeles. What was more unsettling: the boarded-up storefronts on La Cienega Boulevard, or the loss of a patient’s trust? He had weighed my medical expertise against that of the President and found me lacking. Did he really not trust me anymore?

I could not prescribe prophylactic hydroxychloroquine based on wishful thinking. As every student of clinical trials knows, the path to bad outcomes is paved with plausible surrogate endpoints. Ask anyone who ever administered flecainide to suppress premature ventricular contractions (PVCs) after myocardial infarction, post-menopausal hormonal therapy to improve lipid profiles, or thiazolidinediones to reduce hemoglobin A1c in diabetic patients. Reducing the burden of PVCs, the level of low-density lipoprotein cholesterol, and hemoglobin A1c are noble goals, yet medications to effect these changes result in arrhythmic death,¹ coronary heart disease,^{2,3} and heart failure.⁴

Then, all at once, as I sped through the rare green light at Crescent Heights and Sunset Boulevard, I remembered how scared he was, in that Italian hospital years prior, and how my voice on the phone had been enough to comfort him. As scared as he was then, he was more so now. He might have requested hydroxychloroquine, but what he needed was reassurance. He had asked for comfort and I had responded with science. As a different President, Teddy Roosevelt, said, “Nobody cares how much you know until they know how much you care.” And this time, I had failed to convince him that I cared.

I reached out a few days later. I told him that while I could not prescribe prophylactic hydroxychloroquine, I understood why he wanted it. I validated his unspoken fear: as an older man with a cardiac condition, he was at risk of fatal respiratory failure from COVID-19. I expected that voicing his greatest fear might upset him more; instead, he was relieved that I did not minimize the danger.

I explained that while I understood his fear, I could not be swayed by it. As physicians, our decisions must be based on available evidence, not on hope or panic. What if, after I

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declined to prescribe hydroxychloroquine, he died of COVID-19, and, months later, hydroxychloroquine was proven effective as prophylaxis? On the other hand, what if I gave in and prescribed hydroxychloroquine, he took it for the sniffles, and suffered fatal polymorphic ventricular tachycardia? The former would be tragic but the latter would be unforgiveable.

I did not expect to change his mind, and I was not surprised when he called me a week later to let me know that he had obtained a stash of hydroxychloroquine. The tension between anecdotes and data, between giving a patient what they want versus what they need, has always threatened to break the trust between patients and physicians. COVID-19 simply heightens these tensions. With the risk of imminent death and the lure of unproven wonder drugs, reason can fall prey to emotion. But there was a small silver lining: he promised that he would not take any hydroxychloroquine without contacting me first, and I believed him.

He ended our call by asking, "Are we okay?" He too sought to repair our fractured trust. I had science on my side, but he had the fear of death on his; we could disagree on the best way to remain safe in the pandemic and still

trust each other. The fear and uncertainty of COVID-19 may strain the patient-physician bond, but it need not break it. Patients need to know that we, as physicians, will not abandon them if we disagree. When this pandemic ends, our trust will be stronger for it.

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References

1. Echt DS, Liebson PR, Mitchell LB, et al. Mortality and Morbidity in Patients Receiving Encainide, Flecainide, or Placebo — The Cardiac Arrhythmia Suppression Trial. *N Engl J Med* 1991;324:781–8.
2. Manson JE, Hsia H, Johnson KC, et al. Estrogen plus Progestin and the Risk of Coronary Heart Disease. *N Engl J Med* 2003;349:523–34.
3. Nissen SE, Wolski K. Effect of Rosiglitazone on the Risk of Myocardial Infarction and Death from Cardiovascular Causes. *N Engl J Med* 2007;356:2457–71.
4. Singh S, Loke YK, Furberg CD. Long-term risk of cardiovascular events with rosiglitazone: a meta-analysis. *JAMA* 2007;298:1189–95.