FDA Pulls the Plug On Malaria Drugs For COVID. It Was Inevitable.

By Josh Bloom — June 15, 2020

Perhaps someday a ballad will be written about the tragic tale of hydroxychloroquine (HCQ) and its ugly cousin chloroquine (CQ). HCQ, a potential (and controversial) therapy for COVID-19 at one time, is no more. The FDA revoked the emergency authorization of both HCQ and CQ. This was an example of how NOT to develop a drug. A lesson learned -- or not.

The FDA just revoked the emergency authorization of chloroquine and hydroxychloroquine (HCQ) - two malaria drugs that were supposed to help control coronavirus infection. But they were strong on hype and weak on results. The agency said that the two drugs are "unlikely to be effective" and it’s about time.

If there were a course on the wrong way to determine the utility of a drug this episode would be a must. People of various disciplines were standing on their collective heads in order to find some use for hydroxychloroquine (brand name Plaquenil) as a weapon against coronavirus. They put up a good fight – so much so that a global shortage of HCQ (used for lupus and malaria) resulted and people were gulping down pills that not only didn’t work but also had a downside - cardiac toxicity, something I wrote about in May. (See The Real Problem With Hydroxychloroquine Is Nothing New. It's Chemistry [1].)
The unseemly campaign has earned in a chapter in a non-existent book called "10 Ways to Screw Up Drug Development." Specifically, the utility of the drug became a political issue (how stupid is this?), and the basis of a bunch of conspiracy theories (ditto). Throw in a truckload of uncontrolled clinical trials, some of which were little more than a joke, a retracted paper, individual agendas, some patient testimonies, and finally - a controlled clinical trial [2] that showed that HCQ didn't work for post-exposure prophylaxis, and voila - the end of the clown show and the perfect recipe for making a bad drug look good. It could have also been the other way around. Foot stomping, no matter how loud, doesn't influence pharmacology.

In reality, the announcement, which resulted from a letter, written by the FDA’s Denise M. Hinton to BARDA (1), was mostly a moot point. The use of HCQ has been plummeting for some time [3].

Unfortunately, you could see this coming some time ago. I, like every other marginally sane person on earth, desperately wanted a pill that could diminish the severity of the disease, perhaps turn it into something like a "mild flu" rather than the monster it is. Being in a high-risk group and having an aversion to ventilators (as well as death), I was rooting for HCQ while at the same time having doubts about it.

In early March I noted that chloroquine was unlikely to do the job [4], largely because its in vitro cell activity (ability to stop the virus from replicating in cultured cells - was weak). Result: I had a bunch of people screaming at me.

In late March I took a look at hydroxychloroquine [5]. It looked much better than chloroquine regarding cell toxicity, so it is not surprising that it has a better safety profile. But antiviral potency was still a problem. Although the numbers varied widely from lab to lab, HCQ was also a weak inhibitor or viral growth in cells. It was more hopeful because a larger dose could be given but there was nothing impressive about the compound. Also, the quality of the evidence that the drug worked in the clinic ranged from hideous to ghastly. Result: even more people were screaming at me.
In May I explained why HCQ can cause arrhythmias [1] (irregular heartbeats) by showing that the drug binds to voltage-gated ion channels (pores in cells that control electrical impulses) and screwing up the normal heart rhythm. Yes, people screamed at me, but maybe they quieted down when a large epidemiological study in The Lancet showed that more people who took HCQ died from ventricular arrhythmias. But they may have started screaming again when the paper was retracted [6].

What a mess. This unfortunate episode should (but probably won't) teach us that "science by hysteria" is unlikely to result in anything more than confusion and people screaming at me.

So, it's RIP for HCQ. Fortunately, NHC is looking pretty good at the moment. I sure hope so because we are going to run out of acronyms. Or maybe not. A Wisconsin psychiatrist recently asked the FDA to grant emergency approval for LSD [7] ASAP to treat to help patients cope with depression, anxiety, and PTSD brought about by COVID.

That's no BS.

NOTE:
(1) BARDA is (another) acronym for the Biomedical Advanced Research and Development Authority. It is part of HHS.