Put Your Money on a COVID Drug, Before a Vaccine

By Josh Bloom — May 27, 2020

Currently, COVID-19 vaccines are all the rage. Expectations are not only high, they are too high. ACSH friend, and former trustee, Dr. Paul Offit gives us a much-needed reality check. A vaccine, especially a very effective one, is unlikely to be in the cards anytime soon. Although it is always better to prevent an infection than treat one, antiviral drugs are likely to be the tools to control coronavirus well before a vaccine appears. Here’s how Dr. Offit sees this playing out.

In the pharmaceutical industry, there’s a low-level Hatfield-McCoy thing between chemists and biologists that’s been going on forever. Each group thinks that the other group is a bunch of morons. This is fine, but when they try to do each other’s jobs things don’t go so smoothly.

Here’s an example from the 1990s, which didn’t exactly help my financial remuneration that year (1).

Setting:
Discovery team meeting – a two-hour exercise in endurance, masochism, and listening to people
blather on forever. But the meetings are not all boring. This one wasn't.

Here's an example in which the chemistry team leader (yours truly) and the biology team leader (major dimwit) had a less-than-professional exchange.

1. Biologist team leader presents the results of the screening of a few thousand compounds that might be of some use in treating (it really doesn't matter) and informs the team that they had selected what they thought to be a viable candidate. So, naturally, they were going to initiate some studies in mice. Without bothering to consult a single chemist.

2. Chemist (me) looks at the chemical structure of the "best candidate" in utter disbelief. It is so obviously toxic that I cannot believe what I'm seeing/hearing (2). The phrase "these guys must sure like poisoning mice!" may have crossed my mind.

3. Since I pride myself in my ability to bring together different points of view in a calm, gracious manner, I offered what I thought was a perfectly reasonable, time-saving suggestion: "Why don't you just paint the stuff on a bullet and fire it into the mouse? The results will be the same."

Astute observers may have noted a subtle change in the tone of the meeting. While other chemists are peeing themselves in uncontrolled spasms of hilarity, the biologists are glaring at me with poorly disguised hatred.

4. Despite (or in spite of) my respectful, professional advice they go ahead and give the stuff to mice anyhow.

Two days later:

Photo: Istockphoto, Riken news [1]

So, it's fairly safe to say that biologists and chemists see things differently and even safer to say that vaccine scientists and chemists don't even exist on the same astral plane. We just don't get each other. But there is (at least) one notable exception, former ACSH trustee Dr. Paul Offit, the Director of the Vaccine Education Center and professor of pediatrics in the Division of Infectious Diseases at Children's Hospital of Philadelphia. Pennsylvania.

Offit is the inventor of RotaTeq® one of the two US approved rotavirus vaccines (3), which has saved hundreds of thousands of lives around the world, especially in developing countries where access to rehydration is limited. He is brilliant and a hero in the world of public health. And an all-
around good guy too.

So, you ought to listen to his recent brief interview with John King on CNN. It is a two-minute reality check. In case you don't have two minutes, here is the gist of what Dr. Offit has to say:

- On the current crop of experimental vaccines: "These are extraordinarily preliminary results. What we are waiting for is the big trial - a large, prospective placebo-controlled trial [with] 20,000 people who get a vaccine, 10,000 people who get a placebo."
- Getting an answer: "Then and only then will you know if a vaccine is safe and effective."
- Will it work? "I'd be really surprised if that happened by the end of the year. You'd have to be really lucky."
- (He doesn't bite on King's question on whether President Trump is "too far out there - irrational exuberance or do you think he's OK.) "It's fine to be optimistic and aspirational but this process works in a specific way and it's worked this way ever since the first vaccine was invented."
- Offit is concerned that since we are so terrified of this particular virus we may be willing to "accept something less."
- On expecting too much from the vaccine: "the protection may be short-lived and incomplete" and that it would protect against moderate-to-severe disease, but not mild disease... we need to manage expectations about what to expect from this vaccine."

It is clear that Dr. Offit isn't saying that there won't be an effective vaccine, just that it's not going to be quick or easy to discover and won't be a cure-all. So, what to do in the meantime?

In the long run, the only way to stop the spread of the virus is with an effective vaccine. But getting there won't be easy. Antivirals are at best a stop gap. Prevention is always better than cure.

Paul Offit, MD Private communication

As a chemist, I look at it a little differently. There are many infections that can be prevented by vaccines. And there are some, norovirus, HIV, hepatitis C...others) for which no vaccine exists. Despite four decades of research, there isn't a vaccine to prevent HIV infection, but there are extremely powerful drugs to keep it very well under control. There is also no vaccine for hepatitis C, but new drugs (they took 20+ years to discover and develop) can cure the infection >95% of the time.

In the absence of a vaccine, antiviral drugs can be a very powerful tool. One (remdesivir) has been approved, but it has not lived up to initial expectations. The results on hydroxychloroquine-azithromycin have been mixed at best. Right now we'll take whatever works. What else is out there?

Tomorrow: N-Hydroxycytidine will be stepping up to the plate with a new manager - Merck.

NOTES:
(1) One time my supervisor said that the only thing wrong with me was the lack of a filter between my brain and mouth. So, I replied that was wrong and he should go ####### himself.

**UPDATE 5/28** - Said supervisor emailed me: "I never said that was the only thing wrong with you."

(2) With time, many medicinal chemists develop what we call "eyeball toxicity" - the ability to look at a chemical structure and determine if it’s toxic. We are pretty good at this. But it doesn’t work the other way. It is much more difficult to look at a chemical structure and predict that it’s safe.

(3) Rotavirus is sort of a norovirus that kids get. It causes vomiting and diarrhea. Almost all children get it before they’re 5. There are two approved rotavirus vaccines in the US. The first was RotaTeq (2006). This is the vaccine that Dr. Offit worked for more than two decades. It is sold by Merck. The other is Rotarix (GSK, 2008). These vaccines have cut ER visits and hospital admissions in half in the US and have saved hundreds of thousands of lives worldwide.

(4) For a clinical trial to be able to prove whether a drug or vaccine works it must be studied prospectively, with predetermined outcomes/goals. By contrast, retrospective studies involve looking at data from previous trials. They prove nothing and most of them suck.

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