Everyone take a deep breath and relax. During these crazy times, people are making all kinds of wild predictions about what drug or vaccine will work. Dr. David Shlaes takes a sobering look at the chances for any of these therapies to work. It's not as easy as you'd think. We should all lower our expectations a bit.

I thought that this would be a good time to review the various vaccines and therapies being studied to combat the coronavirus pandemic. In such a short article, it will be impossible to review them all. Additionally, the number under study grows substantially every day so this article might well be out of date when it's published.

First, without trying to throw cold water on all your hopes, we should take a look at the odds. A vaccine or therapy that is found in a laboratory has only a tiny chance of making it all the way to approval by a regulatory agency. Once a vaccine enters the earliest stages of clinical trials (phase 1), usually in healthy volunteers to study safety and get an early read on possible immune response, the chances of ultimate approval are only around 15%. For a therapeutic (like an antiviral drug), those odds are more like 10%. But, if a vaccine or drug makes it all the way to the last stage of clinical testing (phase 3), chances of ultimate approval go up to 75%.
(Disclaimer – I don’t pretend to be a vaccine expert – and I’m not trying to play one on TV. Feel free to challenge my thoughts with your own research or, if you are an expert, respond to the blog).

I’ll limit myself to only a few vaccines either already being studied in the clinic or about to enter Phase 1 clinical trials. None are farther along, hence the long timeline of 12-18 months before anything could reach the marketplace. The vaccine [2] by Moderna that has entered phase 1 is based on mRNA. Once we knew the nucleic acid sequence of SARS-Cov-2 (today’s pandemic virus), the scientists at Modena were able to choose a portion of that sequence that encodes a key viral protein without which the virus would be unable to attack our cells. If such a vaccine could stimulate our immune cells to target that protein, we might be protected from the virus. mRNA vaccine is a scientifically “cool” technology and has promise. Not only is this an early effort, but previous mRNA vaccines have never worked to prevent an infectious disease in humans. The risk of failure is high. The same is true of the vaccine from J&J [3]. It seems to be based on the use of a defective adenovirus (the technology used is not publicly available as far as I can see). Once again, this approach has never worked before in humans. Nevertheless, both Moderna and J&J (with the backing of BARDA) have high confidence in their candidate vaccines. Finally, there is the vaccine announced [4] recently by the University of Pittsburgh. To me, this has the most promise of the three I’m reviewing for you. In this case, they have purified viral proteins and impregnated a Velcro-like device with micro-needles to deliver the proteins. The microneedles inject the viral proteins just under the skin – a target known to provide for a strong immune response. This kind of approach has a good precedent for success (micro-needles aside). If they have chosen the right proteins in the right dosage and safety is not a problem, this might work.

I am optimistic that we will have an effective viral therapy before we have a vaccine. The first and most promising drug being studied is remdesivir from Gilead Pharmaceuticals. This drug is an analogue of the building blocks of the viral nucleic acid and stops viral reproduction dead in vitro. It has also worked in animal models of coronavirus infection including mice and monkeys. Because remdesivir was originally studied against Ebola in clinical trials, we already have a significant safety database suggesting that safety in humans will not be a problem. Unfortunately, the drug did not work for Ebola. But it currently is in phase 3 trials [5] for coronavirus looking at patients with both severe and mild to moderate disease. There is also an expanded access program available through Gilead in various centers around the world. The drug can only be given intravenously. This will be a disadvantage since, based on our experience with other antiviral drugs, it is most likely to when given early to those with mild to moderate disease.
Favipiravir, that is similar in concept and mechanism to remdesivir, is an orally bioavailable drug, and is approved for use in the treatment of influenza in Japan. Favipiravir is a rather broad-spectrum antiviral drug with activity in vitro against Ebola and SARS-cov-2. Here, we have much less data. But the drug is already in phase 3 trials for treatment of coronavirus infection based on its approved use for the treatment of influenza and a large safety database.

A discussion of drugs against coronavirus would not be complete without talking about chloroquine, hyxroxychloroquine (plus or minus azithromycin). These are not direct-acting antiviral drugs. All work by trying to improve the host response to viral infection. To say the least, the data here are incomplete and controversial. I have found four small studies using these drugs singly or in combination. Two suggest that there might be efficacy and two find no effect – especially in moderate to severe disease. Only one paper has been peer-reviewed so far. All studies are too small to allow for any sort of statistical comparison between treatment groups. Here I must agree with Dr. Fauci and others who suggest that these drugs should be reserved for those who can benefit from them – patients with lupus and rheumatoid arthritis. Panic buying will expose the public to counterfeit drugs and will deprive patients with legitimate needs of these drugs in order to live a normal life.

All the other therapeutics are well behind the two drugs cited above. A number of companies are studying the use of monoclonal or polyclonal antibodies for the treatment of coronavirus disease. This is a promising approach that is generally well behind the antiviral drugs I noted above. Immunity will probably depend on antibodies and antibodies are probably mainly responsible for clearing the viral infection. Afflicted patients are currently being studied using convalescent plasma from patients who have survived infection. If we can achieve sufficient antibody titers with this approach, it could save lives. It would be important, as always, to treat early. We should have an answer for these studies soon.

I hope this brief and incomplete review puts some of the vaccine and therapeutic approaches to coronavirus infection in some perspective. For a recent, more complete (and more technical) review see this excellent article by Miguel Martinez. Also see the analysis provided by Alan Carr of Needham.

Reprinted from Dr. Shlaes' blog] [10] Antibiotics, the Perfect Storm.