CITY JOURNAL

FROM THE MAGAZINE

A Cure for the Common Misconception

Covid-19 vaccines are possible, but we need a public-health mind-set to make the most of them.

Peter Kolchinsky

Spring 2020

It will probably take at least 18 months, but the biopharmaceutical industry will surmount the technical challenges to create a vaccine for Covid-19. Some think that's not possible, since we haven't created vaccines to the four human coronaviruses that regularly cause common colds. This is a misconception.

The lack of a vaccine against those viruses is hardly because of technical challenges. We can make a vaccine against a coronavirus—we've even got several for chickens. The reasons we don't vaccinate against human coronaviruses explain a lot about the economics of clinical development and the way we think about drugs, vaccines, and risk as patients. They also illuminate why drug companies seem to respond to certain therapeutic challenges, while ignoring others.

Our four standard human coronaviruses cause only 20 percent of colds. The other 80 percent are mostly caused by rhinoviruses, respiratory syncytial virus, parainfluenza virus (not the same as influenza), and other viruses we haven't even identified yet. They are all so different that each would require a different vaccine. So while we could have made a coronavirus vaccine (which might have had to be four vaccines, one for each strain), the trouble is that it would have helped protect against only 20 percent of the viruses that cause colds.

So even if that vaccine reduced your risk of suffering a coronavirus-mediated cold by 75 percent (a pretty good result), that would cut the total risk of getting any cold by only 15 percent (75 percent of 20 percent). It would have to be a large trial, so that we would know that this 15 percent reduction was not due to chance, but it's still doable (even if it might take a few years and be expensive to run). The bigger problem is the marketing message: "Cuts common colds by 15 percent!" isn't exactly compelling, right? Adults get two to four colds a year, some of which they might hardly notice, so a 15 percent reduction doesn't even add up to one fewer cold per year, on average.

People want a common-cold vaccine that protects them against most of their risk. For that, a vaccine would have to protect against most cold viruses (and we don't even know what causes 20 percent to 30 percent of colds), which means that we're really talking about more than a dozen different vaccines that would each require its own development and optimization. We've developed such vaccine "panels"—mixtures of vaccines given in a single shot for measles/mumps/rubella (MMR) and tetanus/diphtheria/pertussis (Tdap)—but each building block of those combinations was useful on its own. They were developed separately and combined for convenience later. But a coronavirus common-cold vaccine would not be useful enough on its own. Nor would a vaccine for rhinoviruses. They're only useful as a set, so that they could collectively make a meaningful dent in one's risk of getting the common cold. Basically, we either succeed in making vaccines for all the major cold viruses, or we shouldn't bother with any. That's daunting. And if we did create such a common-cold vaccine, it would have to be administered each year, like a seasonal flu vaccine, because some of these viruses mutate and because our immune responses to some dissipate over time.

Still, let's say all that can be done—are you going to get the common-cold vaccine, even an awesome one that would reduce the number of colds you get each year in half? Honestly, probably not. It's just a cold! Take a Sudafed and plow on, right? And of course, who likes needles? The common cold is not the public-health threat that flu is, so insurers won't be pressured into making that vaccine affordable to everyone. They'll slap a high copay on it to dissuade you from bothering with it.

And worst of all, the common-cold vaccine would fall victim to the lies of anti-vaxxers. Examples of people being diagnosed with cancer or arthritis or multiple sclerosis in the days or weeks after receiving the common-cold vaccine would be easy to find, just based on random coincidence. Anti-vaxxers would pounce. No matter that data would demonstrate that there's no link between the vaccine and these conditions, many people will think: "why risk it, I'll get over a cold."

The flu is much worse than the common cold, and yet, less than half of Americans get the seasonal flu vaccine that the CDC recommends for everyone, even when it's free, for some of the other reasons I've noted here. Even 10 percent to 25 percent of health-care workers (stats vary by role) skip the flu vaccine each year, though all should know better.

So who's going to foot the bill for development of such a complex multi-virus cold vaccine, given all these risks that it will be a commercial flop? It's not a priority for our government (which understandably prioritizes funding for pandemic flu strains and Ebola). Why would people who manage money on behalf of pension funds, endowments, and millions of ordinary Americans make these kinds of unprofitable investments? Investors look at all this and see a multibillion-dollar sinkhole of risk.

And the common-cold vaccine isn't the only one that investors are hesitant to fund. In 2002, drugmaker GlaxoSmithKline discontinued marketing of its vaccine against Lyme disease, for some of the fear-based reasons above, citing lack of demand after more than a decade on the market. That's a shame, because ticks are spreading, Lyme disease is a brutal condition for many people and hard to cure in some, and the vaccine, LYMERix, was effective at preventing it (it offered a greater than 80 percent reduction in risk after three injections). So we have a Lyme vaccine for dogs—but not one for people.

But back to Covid-19. It is hardly the common cold. In fact, it's way more serious than the flu and feels more urgent and is more ubiquitous than Lyme. So we'll develop a vaccine for it, just as we have for the flu. It might cost a few billion dollars across a dozen different programs to ensure that one or more succeed, but that cost won't matter: there will be a market. And that market is likely here for the long run, since it's doubtful we'll eradicate SARS-CoV-2, the virus that causes Covid-19.

Just as several companies compete for a share of the global $4 billion flu vaccine market, supplying the world with a constantly evolving yet affordable seasonal flu vaccines, we'll eventually have affordable Covid-19 vaccines, likely from several manufacturers. Some companies might even create a combined Covid/flu vaccine, for convenience, since we may need to get a Covid-19 shot every year (immunity to coronaviruses wanes, and the virus may mutate). Also, compared with trials for a common-cold vaccine, Covid-19 trials will be comparatively easy, small, and short, since the disease is caused by only one virus (SARS-CoV-2) instead of a dozen, like the common cold, and recruitment into those trials will be quick due to the global pandemic. With some Covid-19 vaccine candidates already in clinical trials, we'll likely hear soon whether any are promising.

America can be heartless in its poor coverage of many medicines, like insulin (I wrote a book about drug affordability and how to fix our system), but America is pretty good about making vaccines affordable. The flu vaccine typically costs $10 to $20 per dose, though some specialty ones cost a bit more; insurance plans usually cover the cost without a copay. Those without insurance can get a free shot at a flu clinic. Given the public-health concern, a vaccine for Covid-19 would likely be similarly free or affordable to everyone.

And people will be motivated to get a Covid-19 vaccine. Because of the serious public-health implications of Covid-19, there will be no shortage of public-awareness campaigns urging people to get vaccinated. Some employers will even offer it onsite to employees, as many do today with the flu vaccine.

I'll close with an insight from the flu, what it means for Covid-19 vaccine development, and how effective one might be for those who need it most. A vaccine is like a mugshot of a criminal that you can show to police, so that they know who to look out for. As we get older, our immune systems weaken, and vaccines don't work as well; they don't see the mugshot as clearly and can't chase down the criminals in the mugshots as quickly or effectively. The biotech industry is working on vaccines that compensate for our aging immune systems, essentially creating better and clearer mugshots so that more immune cells can join in the hunt. We'll need to employ that advanced technology for Covid-19, given its disproportionate toll on the elderly.

If we end up making a vaccine that works well in children and most adults but not so well in the elderly, we can still protect everyone through herd immunity. If everyone got the Covid-19 vaccine—even those young, healthy people convinced of their immortality—then we'll rob the virus of hosts and insulate our most vulnerable people from getting exposed to the virus. It's a travesty that tens of thousands of Americans, mostly older Americans, die from flu each year, and even more are hospitalized,

partly because the young don't think that they need to vaccinate themselves. When crowds still pack beaches and bars remain full, despite calls for social distancing to stop Covid-19, it's clear that our society still has a long way to go.

So while it may take another year and a half to make a Covid-19 vaccine, we'll need that time to teach everyone about the importance of vaccination to generate the herd immunity that will help protect those with weak immune systems. And maybe we'll then also see an uptick in flu vaccinations, as the young realize that they should get it for others, if not for themselves.

If we don't squander this opportunity to learn and implement a vital lesson on the importance of herd immunity, we may someday remember this crisis as a turning point in our attitude toward vaccines, which may ultimately save more lives than Covid-19 will claim.

***Peter Kolchinsky**, a biotechnology investor and virologist, is Managing Partner of RA Capital Management, L.P., and author of* **The Great American Drug Deal**.

Photo by Sylvain Lefevre/Getty Images

RACAPITAL
RA CAPITAL MANAGEMENT, L.P.

General Disclaimers

The information contained herein (the "Materials") is provided for informational and discussion purposes only and contains statements of opinion and belief. The Materials are not, and may not be relied on in any manner as, legal, tax, or investment advice. The Materials do not constitute an offer to sell, a solicitation to buy, or a recommendation for any security, nor do they constitute an offer to provide investment advisory or other services by RA Capital Management, L.P. and its affiliates and/or any investment products it advises (collectively, "RA Capital" or the "Firm"). Each recipient should make its own investigations and evaluations of RA Capital, and any investment products it advises, and should consult its own attorney, business adviser, and tax adviser as to legal, business, tax, and related matters thereto. The information contained in the Materials is not intended to be, and should not be viewed as, "investment advice" within the meaning of 29 C.F.R. §2510.3-21 or otherwise.

Any views expressed herein, unless otherwise indicated, are those of RA Capital as of the date indicated, are based on information available to RA Capital as of such date, and are subject to change, without notice, based on market and other conditions. No representation is made or assurance given that such views are correct and such views may have become unreliable for various reasons, including changes in market conditions or economic circumstances. Such views may have been formed based upon information, believed to be reliable, that was available at the time the Materials were published. Certain information contained herein concerning economic trends and/or data may be based on or derived from information provided by independent third-party sources. RA Capital believes that the sources from which such information has been obtained are reliable; however, it cannot guarantee the accuracy of such information and has not independently verified the accuracy or completeness of such information or the assumptions on which such information is based. RA Capital has no duty or obligation to update the information contained herein.

The content of the Materials neither constitutes investment advice nor offers any opinion with respect to the suitability of any security. Any references, either general or specific, to securities and/or issuers are for illustrative purposes only and are not intended to be, and should not be interpreted as, advice or recommendations to purchase, continue to hold, or sell such securities, or as an endorsement of any security or company. Certain current and prior investments may be highlighted in order to provide additional information regarding RA Capital's investment strategy, the types of investments it pursues, and current or anticipated exit strategies. In addition, due to confidentiality restrictions, the information contained herein might not reference investments in certain companies. Accounts managed by RA Capital may invest in certain companies referenced in the Materials; however, RA Capital makes no guarantees as to accuracy or completeness of views expressed in the Materials. Any strategies and companies referenced in the Materials may not be suitable for all investors.

As stated above, the Materials are not an offer or solicitation for the purchase or sale of any security, including any interest in RA Capital Healthcare Fund, L.P. (the "Master Fund") or RA Capital Healthcare International Fund Ltd. (the "Offshore Fund," and, collectively with the Master Fund, the "Fund"), and should not be construed as such. Such an offer will only be made by means of a confidential Private Placement Memorandum (the "PPM") to be furnished to qualified investors upon request. The information contained herein is qualified in its entirety by reference to the PPM, which contains additional information about the investment objective, terms, and conditions of an investment in the Fund, and also contains certain disclosures that are important to consider when making an investment decision regarding the Fund. In the case of any inconsistency between any information contained herein or in the Materials and the PPM, the terms of the PPM shall control.

The Materials are proprietary and confidential and may include commercially sensitive information. As such, the Materials must be kept strictly confidential and may not be copied or used for an improper purpose, reproduced, republished, or posted in whole or in part, in any form, without the prior written consent of RA Capital. The recipient of the Materials must not make any communication regarding the information contained herein, including disclosing that the Materials have been provided to such recipient, to any person other than its authorized representatives assisting in considering the information contained herein. Each recipient agrees to the foregoing and to return (or destroy upon RA Capital's instructions) the Materials promptly upon request.

Any investment strategies discussed herein are speculative and involve a high degree of risk, including loss of capital. Investments in any products described herein and the Fund's performance can be volatile, and investors should have the financial ability and be willing to accept such risks. An investor could lose all or a substantial amount of his or her investment. The Fund may be leveraged. Interests in the Fund are illiquid, as there is no secondary market for the Fund interests, and none is expected to develop. The Fund interests are subject to restrictions on transfer. Prior to investing in the Fund, investors should read the PPM and pay particular attention to the risk factors contained therein. Fees and expenses charged in connection with an investment in the Fund may be higher than the fees and expenses of other investment alternatives and may offset investment profits of the Fund. RA Capital has total trading authority over the Fund. The use of a single advisor applying generally similar trading programs could mean lack of diversification and, consequentially, higher risk. A portion of the trades executed for the Fund may take place on foreign exchanges. It should not be assumed, and no representation is made, that past investment performance is reflective of future results. Nothing herein should be deemed to be a prediction or projection of future performance. To the extent any prior or existing investments are described, RA Capital makes no representations, and it should not be assumed, that past investment selection is necessarily reflective of future investment selection, that any performance discussed herein will be achieved or that similar investment opportunities will be available in the future or, if made, will achieve similar results.

In particular, to the extent valuation information is provided for any unrealized investments, such valuations are RA Capital's estimates as of the date set forth in the Materials, and there can be no assurance that unrealized investments will be realized at such valuations. While RA Capital believes any valuations presented herein are reasonable, such valuations may be highly subjective, particularly for private investments, and are based on information provided by third parties and/or RA Capital's assumptions, any or all of which might be mistaken or incomplete. Actual realized returns will depend on, among other factors, future operating results, the value of the assets and market conditions at the time of disposition, any related transaction costs, and the timing and manner or sale, all of which may differ from the assumptions on which the valuations contained herein are based. As a result of the foregoing, actual realized returns may differ materially from the valuations contained herein.

Certain information contained in this document constitutes "forward-looking statements," which can be identified by the use of forward-looking terminology such as "may," "will," "should," "expect," "anticipate," "target," "project," "estimate," "intend," "continue," or "believe," or the negatives thereof or other variations thereon or comparable terminology. Due to various risks and uncertainties, actual events or results or the actual performance of any investment may differ from those reflected or contemplated in such forward-looking statements. Prospective investors should not rely on these forward-looking statements when making an investment decision.

None of the information contained herein has been filed with the U.S. Securities and Exchange Commission, any securities administrator under any securities laws of any U.S. or non-U.S. jurisdiction, or any other U.S. or non-U.S. governmental or self-regulatory authority. No such governmental or self-regulatory authority will pass on the merits of any offering of interests by RA Capital or the adequacy of the information contained herein. Any representation to the contrary is unlawful. The interests in the Fund have not been, and will not be, registered under the U.S. Securities Act of 1933, as amended, or qualified or registered under any applicable state, local, provincial, or other statutes, rules, or regulations. The Fund has not been, and will not be, registered as an investment company under the U.S. Investment Company Act of 1940, as amended.