The Free Market Isn’t Up to the Coronavirus Challenge

BY
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If it’s not profitable for pharmaceutical companies to produce a cure, they won't produce a cure. We cannot win the fight against coronaviruses and future infectious diseases unless we properly fund a public sector that values public health over profit.

Amid all the breathless reporting on the Wuhan coronavirus outbreak, one quote in *Nature* from one of the world’s leading experts on this family of viruses, structural biologist Rolf Hilgenfeld, stood out.

“The total number of people infected, if you combine SARS, MERS [previous related coronavirus outbreaks] and this new virus, is under 12,500 people. That’s not a market. The number of cases is too small. Pharmaceutical companies are not interested,” he told the scientific journal.

Hilgenfeld was on his way to Hubei province even as the Chinese government was placing the 57-million population of Wuhan and surrounding cities under lockdown, or *fēng chéng*, to test early-stage drug candidates on animals infected by the new coronavirus, designated 2019-nCoV.

He had been asked how quickly it would take to complete preclinical testing, and ultimately, assuming positive results, how soon such a response to the disease might be ready for deployment. But his answer suggested that this sort of misses the point, because by the time an effective drug might be ready, it would be too late, not just this time, but whenever these sorts of events happen. The problem is that once a compound is ready to go, by that point, an outbreak may be over.

Why would any company make such a huge investment in drug discovery, only to find at the end that there were no patients?

There is the possibility of performing research on coronaviruses in general and developing

antiviral coronavirus therapies for many coronaviruses — which are also responsible, along with many other viruses, for the illness we collectively call the common cold — instead of just this particular one well ahead of such an outbreak, so as to have a decent head start when a novel coronavirus event does occur.

Indeed, this sort of preparative work is precisely what he and his colleague University of Hong Kong microbiologist Malik Peiris argued was necessary in a 2013 review paper on lessons learned from ten years of research into highly pathogenic coronaviruses, in particular from the SARS and MERS outbreaks. In that paper, he cheered the huge progress that had occurred into the function and structures of the SARS coronavirus, including some research into vaccine development and evaluation on animal models. But after the outbreak waned, by 2005, there was "no incentive to further develop SARS-CoV vaccines." No money either for development of antivirals (for people who have already been infected by the virus). That is, there is no money to be made.

But it's not just the private sector. He took funding agencies to task as well. He did not explain why, but we might: it is not surprising that a neoliberalized public sector in which tax cuts to corporations and the wealthy are prioritized over human need will also find that the cupboard is bare when it comes to diseases that only kill a few tens of thousands.

And perhaps fair enough. For a given size of pie, there are only so many decent-sized slices to go around. Hilgenfeld conceded that virologists themselves likely failed to take the threat of the reemergence of a SARS-like virus sufficiently seriously.

But then the MERS coronavirus hit in 2013, killing some 850 people. Researchers and public health officials were now increasingly cognizant of the potential threat from this family of illnesses.

In 2016, Alimuddin Zumla, a professor of infectious diseases and international health at University College London, argued in a paper that the continuing threat of coronaviruses in the wake of the MERS outbreak presented a "golden opportunity" to overcome the obstacles to the development of anti-coronavirus drugs. He called for the creation of an international collaborative network combining clinicians, virologists, and drug developers backed with political commitment to carry out clinical trials on anti-coronavirus drugs that have already been shown to be safe and effective in vitro (popularly described as 'test-tube experiments') and in animal models.

Zumla echoed Hilgenfeld's concerns that the waxing and waning of numbers of new patients made recruitment for clinical trials difficult and "reduced the incentives for pharmaceutical companies to develop antiviral drugs," adding that MERS cases being predominantly confined to the Middle East didn't help. There is also a "lack of industrial incentives to develop antivirals for mild infections for other, less pathogenic coronaviruses" — the ones that cause the common

cold.

To be sure, there are other significant challenges specific to coronaviruses that make drug development difficult. Above all, they are one of the most diverse and rapidly mutating groups of viruses, and new strains emerge unpredictably. This means that drugs that target existing coronaviruses may not be effective against new ones.

For SARS and MERS, experiments using animal models such as transgenic mice and non-human primates can only be performed in a few biosafety level 3 (high containment) laboratories, and they are technically exacting to boot. But Zumla also wrote that it was the lack of industrial incentives that was the most important obstacle.

Writing in a 2009 book on disaster medicine, the associate director of the National Infectious Diseases Service at the Veterans Health Administration, Shantini Gamage, and her colleagues also noted the unique challenge of coronaviruses, given that information is learned about the pathogen and the disease as the epidemic progresses. And even if, despite this, research is successful, it is still the case that it generally takes about eight years in the United States to march through clinical trials, approval, and marketing.

But once again, Gamage hit upon the unavoidable challenge that the market just doesn't work here. Referring to coronaviruses such as SARS and MERS, she argued that we cannot win this fight unless the public sector leads the charge: "Factoring in the high cost of drug development, the relatively low numbers of cases of an emerging infectious disease initially, and the chance that the epidemic will end with no further cases, pharmaceutical companies would be unlikely to even initiate the discovery process without government intervention or incentives."

The great news is that Hilgenfeld thinks he and his colleagues might have figured out a way around this amoral indifference of market actors. They have developed compounds that are not just active against coronaviruses, but also a large family of enteroviruses. Some 500,000 children catch one known as enterovirus-71 annually, causing hand, foot, and mouth disease. And if something wins approval for these diseases, the researchers reckon that they can also quickly deploy that same drug when we are hit by the next coronavirus outbreak.

Half a million cases? Now that's market-attractive. "We can get pharma involved," he told the journal.

Let's hope he's right. Three cheers to Hilgenfeld for figuring out a way that may make coronavirus therapeutic development coincide with the profit imperatives of the large pharmaceutical companies. But why should researchers have to bend themselves into knots attempting to make their work coincide with the imperatives of profit-making, especially if such work is in the realm of public health? And what do we do when, for a particular area within public health research, development and deployment (RD&D), there just isn't any way to

shoehorn in profit-making?

The really great news, at least for this particular coronavirus, is that it appears to be only moderately infectious, and it has a fatality rate much lower than SARS or MERS. But at some point in the future, there will be one that *is* more virulent and infectious.

Alongside this, public health officials and researchers are cheering what they describe as unprecedented cooperation, freely sharing sequence data, setting aside egos, and the use of social media (for once playing a positive role!) to facilitate communication between researchers in real time. Scientists are working around the clock. Journals have opened (some) access to relevant papers. Researchers-cum-pirates have used the illegal open-access website Sci-Hub to make more than 5,000 scientific articles relating to coronaviruses fully searchable and free. The initiators of this effort declared: "Dividing the world's scientists with a paywall in the middle of a global humanitarian crisis is an unacceptable and unforgivable act of criminal greed."

As paleontologist and author of *The [R]evolution in Open Science* Jon Tennant put it: "Open Science saves lives." All this extra-market cooperation — or solidarity, the term we on the Left use to describe such selfless, deep humanism — offers a hint of the better world to come, where no one does *anything* for profit any longer, but simply works in service of one another and of the collective advance of freedom.

In other good news, where the Chinese government was widely condemned internationally for its tardiness and secrecy during the SARS outbreak, Beijing appears to have since learned its lessons. The country has been commended by the WHO for the speed, transparency, and competence with which it is tackling the outbreak. (Although fresh reportage from the *New York Times* suggests that officials could be doing even more.)

In addition, in the wake of the SARS outbreak, and following on from the challenges faced in dealing with Ebola in West Africa, a raft of new global partnerships, including the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC), the Emerging Diseases Clinical Assessment and Response Network (EDCARN), the Global Research Collaboration for Infectious Disease Preparedness (GLOPID-R), and the WHO R&D Blueprint, have been established. They straddle the public-private divide, explicitly recognizing that the market, left to its own devices, is insufficient in dealing with these new threats. The establishment of such partnerships, networks, and mechanisms has long been one of the primary recommendations of public health officials. This is undoubtedly a massive step forward.

Another of these networks, the nonprofit public-private Coalition for Epidemic Preparedness Innovations (CEPI), was launched in 2017 to develop epidemic-preventing vaccines and antivirals independent of this market failure. Last week, it announced some $12.5 million in

funding for a University of Queensland lab, the National Institute of Allergy and Infectious Diseases, and two small US biotech firms, Moderna, Inc., and Inovio Pharmaceuticals, to look at three different pathways to develop vaccines for 2019-nCoV. They aim to have a vaccine ready for human testing in sixteen weeks, down from the years that such efforts normally take.

But even if the CEPI-coordinated strategy confronts no unexpected difficulties, the next step, mass production of a vaccine, would present a fresh challenge that CEPI does not have the resources to tackle. According to the journal *Science*, Inovio's facilities could produce 100,000 doses a year; the Queensland researchers four times that, and Moderna 100 million doses. That sounds like a lot but, as the author of the piece reports, in a worst-case scenario, this would be far from sufficient for the world's population.

Moderna and Inovio stocks may have gone through the roof upon the announcement, but as Mark Feinberg, the head of the International AIDS Vaccine Initiative and former chief scientific officer with American pharmaceutical giant Merck's vaccine division during the last Ebola outbreak, warned medical news outlet *Stat*, "The prospects and the amount of work involved will necessarily take [a small biotech company] away from their core business and the interest of their investors in getting a return on their investment."

And it is not just coronaviruses or other emerging infectious diseases that confront this problem. As covered elsewhere in these pages, the crisis of bacterial antibiotic resistance that humanity faces —which has the potential to undermine much of modern medicine because so much of it, from surgeries to catheters and injections to even many diagnostic procedures, depends upon a background of antimicrobial protection — is primarily a problem of insufficient profitability. If successful, a course of antibiotics is only taken for a few weeks or months at most, and then the patient is cured and stops purchasing those drugs. But with chronic diseases, the patient has to purchase those drugs on a regular basis for the rest of their lives. And so most of the large pharmaceutical companies largely got out of the business of antibiotic research and production more than three decades ago.

Antifungal therapeutics face an identical profitability challenge. An extensive 2019 feature in the *New York Times* by science journalists Matt Richtel and Andrew Jacobs investigated the spread over the last five years around the world of the fungus Candida auris, which is resistant to some or all antifungal medications. Half of all those infected die within ninety days. As a result, this fungus has forced even a renowned British medical center to shut down its intensive care unit. And the paper on the scale of the problem that the reporters depended on for the backbone of their story unsurprisingly lays the blame for the "sparse discovery pipeline" on "a chronic lack of investment in novel antifungal agents" because "most pharmaceutical companies are not investing in antifungals, preferring to focus on other, apparently more lucrative areas."

In 2018, the financial giant Goldman Sachs issued a report that asked, "Is curing patients a

sustainable business model?" The analyst thought that Gilead Science's treatment for hepatitis C, which produced cure rates in excess of 90 percent, offered a cautionary tale. While US sales hit as much as $12.5 billion in 2015, they slid to a mere $4 billion three years later because its "hepatitis C franchise has gradually exhausted the available pool of treatable patients." Infectious diseases in particular pose a challenge to profitability because "curing existing patients also decreases the number of carriers able to transmit the virus to new patients." Cancer, thank god, the report concluded, does not pose this problem (the unsaid corollary, of course, being: we damn well better not find a cure for cancer).

As odious as all this appears, the problem therefore is not immorality or evil, as we often hear, but *amorality*. The market can only ever provide what is profitable. It is utterly *indifferent* to human needs.

So in the end, these RD&D networks that are heroically responding to what they acknowledge is a market failure are in the end just very advanced forms of charity — a sort of well-intentioned, warmhearted corporate subsidy that addresses the symptoms but not the systemic cause of the problem. It is akin to offering drugs to ease a patient's emphysema without telling him to quit smoking.

Instead — or, rather, in addition to this, for these research networks are essential not just for the funds they disburse — pharmaceutical RD&D should be entirely freed from the limitations imposed on it by market amorality. The sector should be taken into the public realm and employ the postal model, where profitable routes cross-subsidize money-losing routes, but in this case, unprofitable drug discovery and manufacture would be paid for by their profitable counterparts.

This is not the predictable ramblings of a democratic socialist. It is rather the recommendation last year of the UK's "superbug tsar," Jim O'Neill, a former chief economist for Goldman Sachs. He suggested that nationalizing drug companies would be the best solution to the antibiotic-resistance crisis, comparing the current situation to the 2008 financial crash that forced the nationalization of the Royal Bank of Scotland.

And, as with that emergency nationalization within the financial sector over a decade ago, today we also don't have a lot of time to wait in the pharmaceutical sector. We already confront a crisis of antimicrobial resistance. And the threat from 2019-nCov could turn out to be moderate, but this may not always be the case with coronaviruses or other emerging infectious diseases.

The executive director of the WHO Emergencies Programme, Michael Ryan, said last summer: "We are entering a very new phase of high-impact epidemics." At the time he spoke, the WHO was tracking some 160 disease events around the world, nine of them at the organization's highest emergency level. "I don't think we've ever had a situation where we're responding to so many emergencies at one time. This is a new normal, I don't expect the frequency of these

events to reduce."

The situation is a product of the confluence of increased travel and trade through the advent of globalization, rapid urbanization, rising wealth in economies such as China and India, as well as climate change, deforestation, and the consolidation of food animal production. In addition to tackling these ecological challenges that contribute to the risk from infectious disease, we need a pharmaceutical sector fit for the twenty-first century.

Quite simply, the free market is holding back the advance of science, medicine, and public health.

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