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What the Response to the AIDS Epidemic Can Teach Us

On Monday, February 24, 2020, I was the guest speaker at an investor dinner in Boston. Some twenty professionals, among the smartest people in our sector and many with scientific backgrounds, were there. We talked about science, biopharma companies, board governance, drugs, stocks, markets, and, of course, we discussed COVID-19. No one was alarmed; no one thought about getting up to go sit at the other end of the room or to avoid shaking hands. The epidemic appeared to be mostly an academic issue. We debated incidence and fatality rates. We were lulled into believing that, even if infected, the vast majority of individuals without obvious comorbidities would have a disease course similar to that of a bad flu.

Two days later, I was the lunch speaker in another meeting, this one in a Greek restaurant in New York City with some forty Greeks, each one seated tightly next to the other. We shook hands, hugged, kissed each other on both cheeks the way Greek men do, and lingered afterward in small groups. At that meeting, I was to speak broadly about the biopharma industry but not unexpectedly, the issue of COVID-19 came up. My message was—be careful, but don't panic; it's manageable.

Two days later, I was on a plane to Greece to spend the weekend with family and then to Delphi to participate in the Delphi Economic Forum. When I turned on my phone upon landing in Thessaloniki on Saturday, February 29, the first emails that popped were those relating to the postponement of the forum. Even though no more than a handful of COVID-19 cases had been reported in Greece, the forum organizers thought it wouldn't be prudent to pack 3,000 people in tight quarters. Accordingly, I changed my return flight to New York for Wednesday, March 4.

The night before I was to depart, I received the first of many emails from my colleagues at Biogen alerting me that a high number of individuals among those who had attended a senior management meeting on February 26–27 in Boston were exhibiting flu-like symptoms. Testing was not readily available to provide a definitive diagnosis, but it was reasonable to assume the culprit was SARS-CoV-2.

That's when the epidemic came home to me. In the space of a ten-day period, the epidemic changed from an academic discussion to a personal problem. Week after week, COVID-19 became a personal problem for many Americans and no longer an item on the evening news.

On the plane on the way back from Europe, I played multiple scenarios in my mind, but mostly I was searching for lessons from the past that could provide insights on what was likely to happen. Viral outbreaks of recent years (e.g. SARS, MERS, Ebola) were not useful. The incidence was low and they all had taken place far away from most of us; this was here, it was near us, it was around us, and the numbers were rising at an alarming pace. I realized then that the closest we had been to something like the onset of COVID-19 was the beginning of the AIDS epidemic in the early 1980s. So how are they similar and how are they different? And what lessons can we derive from studying the past?

In the early 1980s I was on the faculty of the Department of Cell Biology at New York University School of Medicine and my wife was a medicine resident at Bellevue, the flagship public hospital in New York City and what became the epicenter of AIDS patient care in the early 1980s. AIDS awareness began through a series of subtle observations by discerning physicians—a cluster of *Pneumocystis carinii* pneumonia here, an increased number of Kaposi's sarcoma cases there. The common thread appeared to be that these patients seemed to experience an unusually severe disease burden, largely because their immune systems were compromised. Another common thread was that the patients were predominantly male homosexuals. In fact, the early name for AIDS was GRID—Gay-Related Immune Deficiency.

Soon the medical observations from different parts of the country coalesced around plausible hypotheses, retrovirologists went hard at work to identify the culprit virus, diagnostic tests were being developed, and drug and vaccine projects got underway.

But in looking back, it is scary how long it took for real medical advances to be achieved in AIDS. There were social, financial, and scientific reasons for that. Society at large viewed AIDS as a lifestyle disease mostly afflicting homosexuals and IV drug abusers (of the 9,600 patients with AIDS in 1985, only 142 had been infected from tainted blood). Consequently, a self-righteous part of society considered the disease to be just punishment for the sinful. Companies were hesitant to embark on drug research in AIDS—there was concern that, for whatever drug or vaccine was to be invented, the government would have stepped in and demanded wide access at a very low price. But the biggest challenge was the state of scientific capabilities measured against the degree of difficulty of the problem at hand. All these factors conspired to slow progress and, in fact, if it had not been for the efforts of the AIDS activist community, much less would have been accomplished.

The enormous difference between our response to COVID-19 compared with AIDS is the ferocity with which the biopharma sector has committed resources toward solving the problem and the extraordinary progress that has been made in a short time. Yes, science is more advanced today than it was in the early 1980s, but importantly we have a far more dynamic, resource-rich, and morally responsible biopharma industry—a big part of what motivates many of us to work hard in improving the human condition is our sense of duty.

Consider the rate of progress. From 1980–81, when the first AIDS cases were reported in the US, it took until March 2, 1985, for the first diagnostic test, an ELISA-based assay for the purpose of screening blood, to be approved by the Food and Drug Administration (FDA). To ensure the safety of the blood supply, the test was highly sensitive. Consequently, when used to test patient blood for the purpose of offering a diagnosis (for which it was not approved), it resulted in too many false positives. The first rapid HIV diagnostic kit was approved on November 7, 2002, and the first at-home diagnostic kit was approved on July 3, 2012. By comparison, for SARS-CoV-2, under FDA's Emergency Use Authorization, we already have more than one hundred PCR-based virus detection kits as well as serological tests to detect antibodies in patient blood. True, the tests are not as accurate or scalable as we would like them to be, and an antigen test is needed so we can proceed with massive screening, but the progress is still remarkable.

On March 19, 1987, zidovudine (AZT), a compound originally synthesized as a potential anticancer agent, became the first drug approved by FDA to treat AIDS patients. As of the end of April 2020, less than six months since the first reports of COVID-19 from China, more than 300 clinical studies are focusing on repurposed drugs, direct antivirals already studied against similar viruses, novel antibodies, and

convalescent plasma. It is very likely that over the next six to twenty-four months, one or more of these studies will form the basis for the approval of agents that could help improve patient outcomes.

In addition, multiple approaches are deployed for novel vaccine development. Here we would have to be a bit more cautious in our expectations compared to the dialog in media and the general public. It appears that we state axiomatically that we will have a vaccine, and the only question is whether it is six months or twenty-four months away. A vaccine against a novel agent and based on mostly novel platforms is complicated, and it may well be many years before a truly efficacious and safe vaccine is developed. A sobering reminder is that we are in our fourth decade of trying and still do not have an HIV vaccine.

How did the world cope with AIDS during all those years when not much was available for treatment? The panic subsided when we came to understand the biology of transmission. Early in the epidemic the fear of the unknown prevailed. People were concerned about their food being prepared by infected individuals, shaking hands, or being in the same room with them. Medical staff would double-gown and double-glove before entering the rooms of AIDS patients. And the burden to the system was overwhelming. At one point in 1985, a quarter of the 200 medicine beds at Bellevue were occupied by AIDS patients mostly kept in isolation, one patient per room. Worst of all was the fear of accidental pricking by a needle used on an AIDS patient. As it became clear that AIDS patients were more at risk of getting sick from healthy people because of their severely compromised immune systems, rather than infecting those around them through casual contact, the pressure was lifted from society.

The lesson is that it is of paramount importance to understand the biology of transmission of SARS-CoV-2 so we treat those who require treatment and redirect resources away from those who will navigate benignly through a potential infection or are not likely to get infected. The scientific community is well aware of these issues and that what stands on the way of answering the transmission-related question is mostly resources—reliable and scalable diagnostic tests so we can engage in massive testing. In addition, we need the self-discipline to carry out such studies with rigor, sacrificing time in order to end up with scientifically defensible answers.

The current pandemic has had a deleterious effect on economies, and the worst is probably still to come. Restarting economies and redeploying the extremely high number of unemployed will be a challenge, particularly because many of those out of work now will never be able to return to their old jobs, given that many professions and businesses will be redefined. And the crisis will be exacerbated when the virus spreads over the next few months to developing nations, particularly in Africa, where there is limited opportunity for social distancing or tertiary medical care.

The past few months have been a trying time for people in this and many other countries. But not everyone in the US has been affected the same way. Affluent families shelter in place in comfortable suburban homes or weekend retreats, they get food and goods delivered to their doorsteps, and if they get sick, they have ready access to quality health care. Inner-city middle- and lower-middle-class families, now out of work and in many instances virtually insolvent, are trapped in crowded apartments and are far more likely to get infected. Once they fall ill, they end up in overcrowded and under-resourced city hospitals or die at home. The income inequality, already recognized as a significant social issue in this country, has now become a survival inequality. Along with new drugs and vaccines to fight the virus, we need to rethink our health care delivery system to ensure adequate access to all.

Dr. Stelios Papadopoulos is chair of Biogen Inc., Exelixis Inc., and Regulus Therapeutics Inc. In the not-for-profit sector, Papadopoulos is a member of the Board of Visitors of Duke Medicine, a member of the Global Advisory Board of the Duke Institute for Health Innovation, and cofounder and chair of Fondation Santé, a foundation providing research support to biomedical scientists in Greece and Cyprus.

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