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Perspective

COVID-19: an 'extraterrestrial' disease?

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ABSTRACT

Background: Since the beginning of the pandemic, COVID-19 has been regarded as an exceptional disease. Control measures have exclusively focused on 'the virus', while failing to account for other biological and social factors that determine severe forms of the disease.
Aim: We argue that although COVID-19 was initially considered a new challenge, justifying extraordinary response measures, this situation has changed — and so should our response.
Main arguments: We now know that COVID-19 shares many features of common infectious respiratory diseases, and can now ascertain that SARS-CoV-2 has not suddenly presented new problems. Instead, it has exposed and exacerbated existing problems in health systems and the underlying health of the population. COVID-19 is evidently not an 'extraterrestrial' disease. It is a complex zoonotic disease, and it needs to be managed as such, following long-proven principles of medicine and public health.
Conclusion: A complex disease cannot be solved through a simple, magic-bullet cure or vaccine. The heterogeneity of population profiles susceptible to developing a severe form of COVID-19 suggests the need to adopt varying, targeted measures that are able to address risk profiles in an appropriate way. The critical role of comorbidities in disease severity calls for short-term, virus-targeted interventions to be complemented with medium-term policies aimed at reducing the burden of comorbidities, as well as mitigating the risk of transition from infection to disease. Strategies required include upstream prevention, early treatment, and consolidation of the health system.

Background

Although the threat of a pandemic had been present for many years, COVID-19 triggered frantic and uncoordinated reactions worldwide (Independent Panel for Pandemic Preparedness and Response, 2021; Paul et al., 2020b). Since being declared a public health emergency in January 2020, COVID-19 has been regarded as an exceptional disease, almost as if it came from outer space. For the first time in history, billions of people were locked down, denied the right to go to school or to earn their living, and/or to see their loved ones, while an unprecedented race for treatment and vaccine discovery was launched. The collateral damage from these response measures was largely ignored, even if it may have been greater than the positive effects of the implemented policies (Hrynick et al., 2021). It ranged from economic recession and loss of education, to increases in domestic violence and mental health problems, and the worsening of chronic conditions from a lack of access to care (Bavli et al., 2020). The effects weighed particularly heavily on young people, and hit the most vulnerable disproportionately, aggravating inequities (Chakrabarti et al., 2021). In many countries, primary healthcare professionals were denied the right to treat their patients. Without effective primary healthcare, hospitals were left with the task of treating severe cases, notwithstanding the absence of a specific recommended drug. This led

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to the further exacerbation of existing disparities in health systems and services, especially in low- and middle-income countries (Baral, 2021).

Despite the fact that COVID-19 could be categorised as a 'syndemic' (Horton, 2020) — a synergy of epidemics that 'co-occur in time and place, interact with each other to produce complex sequelae, and share common underlying societal drivers' (Swinburn et al., 2019) — control measures were exclusively focused on 'the virus' and delay tactics, while not taking into account other biological and social factors that contribute to determining severe forms of the disease (Paul et al., 2020a). After several inconclusive results, it was only in July 2020 that one of the two large international randomized controlled trials aimed at testing the efficacy of existing treatments against COVID-19 published a preliminary report showing that dexamethasone (a glucocorticoid) resulted, on average, in lower mortality rates in patients requiring supplemental oxygen or invasive mechanical ventilation (The RECOVERY Collaborative Group, 2020). The lack of evidence on more effective medical treatments, coupled with projections suggesting high disease loads and death tolls, led to the perception that this was a one-off disease. This, unfortunately, led to proven and traditional medical and public-health practices being largely ignored. For instance, the longstanding concept of 'herd immunity', which has always represented an objective, or an achievement, is now considered by many as a 'strategy' — not to be acquired naturally, but only through vaccination (World Health Organization, 2020). In spite of all its potential risks, limitations, and considerable uncertainties regarding long-term side effects, the duration of protection, and its effectiveness against viral variants, vaccination quickly became the only salvation option promoted by key governments and international institutions.

Although it is understandable that COVID-19 was considered an exceptional disease in early 2020, justifying exceptional response measures — particularly since SARS-CoV-2 can trigger a variety of symptoms, some of them extremely severe (Hu et al., 2020; Wiersinga et al., 2020) — the situation has changed. So should our response (Paul et al., 2020a). In this article, we argue that now that we far better understand the complex functioning of COVID-19, we should adapt our response strategy in a way that addresses its heterogeneity, and embraces proven and traditional medical and public-health practices.

Analytical approach

Various areas of expertise are relevant to approaching the complexity of the COVID-19 response. This article is based on a collaboration of clinicians, researchers, and experts in public-health policies based in three continents (America, Africa, and Europe) who are concerned by the COVID-19 response strategies in their respective countries — Belgium, Democratic Republic of the Congo, France, Germany, UK, USA — and at the global level. Together, they combine expertise in intensive care practice, biophysics, public health, virology, and health policies and systems. This paper adopts a reflexive analytical approach — where reflexivity can be defined 'as an intentional intellectual activity in which individuals explore or examine a situation, an issue, or a particular object on the basis of their past experiences to develop new understandings that will ultimately influence their actions' (Tremblay et al., 2014) — to critically analyze, from a multidisciplinary point of view, the COVID-19 response strategy at the global level.

COVID-19 exposed existing problems

We now know that COVID-19 shares many features of common infectious respiratory diseases in terms of its transmission process — it is caused by a coronavirus whose transmission is airborne (Greenhalgh et al., 2021). Its immunopathology is better understood (Cao, 2020) and may entail vascular and immune system dysfunctions, possibly leading to a cytokine storm (Garvin et al., 2020; Varga et al., 2020). Its severity and lethality are largely related to age, social determinants, and comorbidities (Williamson et al., 2020), while its infection–fatality rate, which averages around 0.2–0.3%, is extremely low for young people (Ioannidis, 2020; O'Driscoll et al., 2020). Overall, SARS-CoV-2 has not created new problems out of the blue, but rather has exposed and exacerbated existing problems in the context in which it finds itself. For instance, in the USA, COVID-19 has revealed the poor health status of a large proportion of the population, with two-thirds of COVID-19 hospitalizations attributable to four major cardiometabolic conditions (O'Hearn et al., 2021), the critical role of social determinants of health (Karmakar et al., 2021), as well as 'deep underlying problems in the healthcare system' (Blumenthal et al., 2020). In Europe, the pandemic has highlighted the ageing population, a lack of healthcare personnel resources, and the insufficiency of quality primary healthcare (OECD/European Union, 2020). In Brazil, existing socioeconomic inequalities have driven epidemic outcomes more than any other risk factor (Rocha et al., 2021). Above all, COVID-19 has revealed the lack of health-system preparedness for pandemics, with inept global policies, non-existent and outdated national plans, a lack of health-system adaptability, equipment shortages, unreliable availability of medicines, poor communication strategies, fragmented diagnostic capabilities, and poor governance structures (Baral, 2021; Paul et al., 2020b).

Implications for policy

COVID-19 is not an extraterrestrial disease that appeared from nowhere. It is a complex zoonotic disease and it needs to be managed as such (Wernli et al., 2021), following long-proven principles of medicine and public health. A complex disease cannot be solved through a simple magic-bullet cure or vaccine. This especially true when the infectious agent is an airborne virus with not only one, but many animal reservoirs, being a known zoonosis that can be found in numerous species around human habitats (Shi et al., 2020; Ye et al., 2020; Wardeh et al., 2021; He et al., 2021). As a result, claims for its eradication are naïve. In fact, some scientists are suggesting that 'full' herd immunity to end this pandemic is probably impossible because of new variants arising, doubts over whether the vaccines can prevent transmission, signs of waning immunity, and inequities in the global distribution of vaccines (Aschwanden, 2021). This simple fact also renders viral control policies via the increased use of lockdowns unsustainable. According to 50 years of coronavirus research, as well as knowledge accumulated on respiratory viral infections, we should expect new waves of the virus, or of a variant, probably more regularly in fall and winter, particularly in the northern hemisphere (Estola, 1970; Moriyama et al., 2020). This calls for a shift in policy from a 'zero-risk' strategy, which is imposed top–down via 'command-and-control' lockdowns, to 'risk-mitigation' and 'harm-reduction' strategies through educating and empowering people, especially the most vulnerable (Arnold, 2021; Loewenson et al., 2021, 2020).

The heterogeneity of population profiles susceptible to developing a severe form of COVID-19 calls for the adoption of varying, targeted measures, which are able to reach risk groups in an appropriate way. The critical role of comorbidities in disease severity calls for complementing short-term virus-targeted interventions — including prophylaxis in high-transmission settings (Seet et al., 2021) — with medium-term procedures aimed at reducing the burden of comorbidities, as well as SARS-CoV-2 infection-to-COVID-19 disease transition risks, at an early stage. The heterogeneity

of COVID-19 symptoms suggests that we should not simply wait for a specific cure that works 'on average' against SARS-CoV-2, at a late stage of the disease. With such heterogeneity, most people's disease development profiles lie far from the average. Moreover, viral infections follow a well-known path from their entry point to ultimate outcomes, requiring the adaptation of treatment to each patient's stage in infection. It is better to start treating before inflammation sets in and to adapt treatments to individual needs, through primary and patient-centred care. For instance, while it has been known since the first wave that COVID-19 causes blood clots, it is only recently that a study has confirmed that prophylactic anticoagulation treatment is probably 'optimal therapy' for COVID-19 patients (Vaughn et al., 2021). Likewise, we should not delay empirical antimicrobial therapy in cases of suspected co-infection prior to the worsening of clinical conditions; the potential benefits of pre-emptive antimicrobial therapy at the time of COVID-19 symptom onset need to be explored appropriately (Contou et al., 2020; Intra et al., 2020; Rawson et al., 2020; Verroken et al., 2020). This point had already been promoted by Dr A Fauci as a conclusion to the flu pandemics of 2008–2009 (Morens et al., 2008). Evidence is now emerging for the potential effectiveness of repurposed drugs, including ivermectin (Hill et al., 2021), amantadine (Cortés-Borra and Aranda-Abreu, 2021), and cofloctol (Belouzard et al., 2021), as well as nutritional supplementation (Alzaabi et al., 2021; Margolin et al., 2021) and new molecules, such as plitidepsin (Varona et al., 2021), at early stages of disease. More research is required at this level. Furthermore, when dealing with patients with known comorbidities, it would be medically sound and therapeutically helpful to carry out typing of the human leukocyte antigen (HLA) for susceptibility, so as to identify those who truly need swifter and deeper care (de Sousa et al., 2020; Langton et al., 2021).

Vaccines are an important part of the response strategy, but only if they follow a precautionary principle, with continuous appraisal of the benefit–risk balance. Doing so is necessary to maintain confidence in vaccines and to avoid adverse effects — as with vaccines against dengue and the influenza H1N1 pandemic (Forcades i Vila, 2015; The Lancet Infectious Diseases, 2018) — that could reinforce vaccine hesitancy on the part of people who need it most. However, vaccines alone will not solve the COVID-19 pandemic (SARS-CoV-2 variants: the need for urgent public health action beyond vaccines, 2021). Thus, additional complementary strategies are needed, including prevention, early treatment, and the consolidation of the health system (Paul et al., 2021). Even if it is not recommended by the World Health Organization as a 'strategy', innate and already naturally acquired immunity, including T-cell immunity (Braun et al., 2020), must be taken into account when determining the most appropriate response policies, including the assessment of the hypothetical herd immunity threshold advanced by many governments as a precondition for lifting non-pharmaceutical interventions. Indeed, there is now mounting evidence that SARS-CoV-2 infection induces robust immune responses, regardless of disease severity (Nielsen et al., 2021), and that acquired natural immunity is lasting (Hall et al., 2021; Turner et al., 2021). This suggests that individuals previously infected by SARS-CoV-2 are unlikely to benefit from COVID-19 vaccination, so that vaccines can be safely prioritised to those who have not been infected before (Shrestha et al., 2021).

Non-pharmaceutical interventions continue to be implemented in many countries despite progress in vaccinations — even strict lockdowns (e.g. in Australia) — in spite of lack of evidence on their overall efficiency (McCartney, 2020). For example, nearly a year and a half after the beginning of the pandemic, there is still low evidence for the effectiveness of face mask wearing in community settings (Chou et al., 2021). While some studies show that stay-at-home policies may have reduced virus transmission, others show that they have not impacted overall mortality (Agrawal et al., 2021). In any case, non-pharmaceutical interventions must be proportional to overall health needs and chosen to take into account local context specificities and existing alternatives, while aiming to maximize expected benefits for general health outcomes and minimize collateral damage. From this perspective, the most efficient measures probably include limiting mass gatherings, promoting outdoor activities, where transmission is very low (Bulfone et al., 2021), implementing sentinel surveillance and smart testing policies (Flandre et al., 2021), and ventilating public indoor places (Bazant and Bush, 2021).

In terms of the policy landscape, public health policies need to be decided and designed in a transparent way, in collaboration with all relevant disciplines and stakeholders, including populations, and social and healthcare workers, and regularly evaluated to ensure continuous adaptation and improvement (Paul et al., 2020a). Moreover, there needs to be a normative shift in how we think about prevention and preparedness, particularly towards a mindset that understands long-term preventative healthcare as an investment, not an expense. Lastly, it is crucial to move beyond our current understanding of health security, which has traditionally favoured surveillance, exceptionalism, 'countermeasures', and an overreliance on vaccine discovery, often at the expense of routine health. As an alternative, the link between health-system strengthening and health security needs to be articulated more forcefully, with better multilevel governance mechanisms for coordinating efforts, integrating community, national, regional, and global levels (World Health Organization, 2021). If not, then the policy lessons from COVID-19 will have been ignored, and we will once again find ourselves confronting the next pandemic as if it were an unexpected and exceptional disease.

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