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COVID-19: the renaissance of science in the face of adversity

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An Editorial on the Frontiers in Science Lead Article
Standing the test of COVID-19: charting the new frontiers of medicine

Key points

- Unlike previous pandemics, COVID-19 emerged at a time when the world was intricately connected due to vast communication and technological advancements, igniting extensive collaboration and medical innovation.
- Mathematical models and simulation tools proved invaluable for decision-makers to guide planning and responses across various governmental and private sectors, both nationally and globally.
- Developments in omics-based technologies and systems biology are poised to drive advancements in our understanding of vaccinology, targeted treatments, and patient stratification—fostering a true era of personalized medicine.
- By integrating computational analytics, artificial intelligence, telehealth, and digital therapeutics, we have unparalleled opportunities to take advantage of big data for informing personalized medicine strategies in the near future.

Introduction

Since its irruption into our lives 4 years ago, COVID-19 has brought about radical changes, redefining our daily routines. During the darkness of the initial lockdowns, which enveloped us in uncertainties and a sense of urgency, who could have predicted that this unparalleled health crisis would serve as a catalyst for a scientific renaissance? This question is exactly what the lead article by Cauchemez and colleagues in *Frontiers in Science* sought to address (1). By analyzing the principal changes that have occurred over the past 4 years, the article provides important insights into how the COVID-19 pandemic transformed the way we integrate acquired knowledge to advance medical innovation. Moreover, it describes the evolving paradigm in our understanding of health, shifting from a focus on

the individual to embracing a "One Health" perspective, i.e., recognizing the interdependence of the health of humans, animals, and the environment.

A pandemic in the modern era

In the history of humanity, pandemics have been a constant: events that are so powerful they have reverberated across generations and guided our evolution. Unlike its predecessors, COVID-19 emerged at a time when the world was intricately connected due to vast communication and technological advancements. This fortuitous alignment of circumstances served as fuel, igniting extensive collaboration and medical innovation.

This direction of travel was apparent at the very beginning of the pandemic, when the genome of SARS-CoV-2 was sequenced and made freely available to researchers worldwide within a matter of days. This was on 10 January 2020, just 1 week after the virus had been isolated for the first time from a small group of patients with unexplained pneumonia in China. Scientists studying the genomic sequence of the SARS-CoV-2 virus relied on high-performance computing and bioinformatics tools to analyze large datasets of viral genomes. Projects such as the Global Initiative on Sharing All Influenza Data (GISAID) facilitated the rapid sharing and analysis of viral genomic data, enabling real-time tracking of viral evolution.

Exactly 2 weeks later, the first comprehensive report on 41 patients with COVID-19 was published in *The Lancet* (2)—at a time when the true scale of the pandemic was still unimaginable. In hindsight, it is truly remarkable how, within a matter of days, such a comprehensive description detailing the epidemiological, clinical, laboratory, and radiological characteristics of the virus, alongside the treatment and clinical patient outcomes, was provided. This is a true testament to the power of collective knowledge sharing and scientific cooperation.

Interdisciplinary collaboration

As the COVID-19 pandemic began to spread to nearly every corner of the globe, it became apparent that our collective preparedness for events of such magnitude was lacking. With healthcare systems collapsing almost everywhere, a new approach was imperative to comprehend the spread of infection and the potential impacts of crucial interventions, especially in the face of limited data and the necessity for swift decision-making.

This was the right time for experts in epidemiological modeling, behavioral science, ethics, data science, policy analysis, and health economics to join forces and develop mathematical models and simulation tools aimed at predicting the spread of SARS-CoV-2 and evaluating the potential effectiveness of public health measures. While models serve as simplified representations of reality, they have been invaluable for decision-makers to guide planning and responses across various governmental and private sectors, both nationally and globally.

Nonetheless, the pivotal role of these models in policymaking also invited unprecedented media attention and public scrutiny. Given the large impact of these models on the lives of so many individuals, it has been imperative to establish best practices. To this aim, *The Lancet* launched a Commission on Strengthening the Use of Epidemiological Modeling of Emerging and Pandemic Infectious Diseases. This commission aims to address the policy, technical, and communication challenges inherent in modeling. A significant amount of effort has been dedicated to responsible reporting and communicating results to the public health community, policymakers, media outlets, and the general public.

The global scientific response to COVID-19: accelerating discovery

As the world geared up to face an unknown virus with drastic non-pharmacological interventions, such as lockdowns and economic shutdowns, scientists worldwide contributed their knowledge to piece together insights into this new pathogen. As meticulously described by Cauchemez and colleagues (1), the pandemic sparked a significant surge in research across various biomedical science disciplines. Overall, there was an increase of 9% in the number of publications in medical and health sciences between 2020 and 2022, as compared with the expected volume, with roughly 7% of articles during this period being related to SARS-CoV-2.

With such a massive amount of information gathered in just 2 years, how could researchers ensure its dissemination to benefit everyone? Here we find yet another novel approach that has contributed to changing the way science is spread. Every discovery was made available to all as quickly as possible through preprint sites —a practice seldom seen in pre-pandemic times. This facilitated the circulation of vital information before data underwent rigorous peer review and scrutiny, which ensures the integrity of scientific findings. And once articles were published, most journals adopted a culture of open access to allow information to be distributed as widely as possible, accelerating not only the pace of discovery but also fostering a spirit of collective progress. The COVID-19 Open Research Dataset (CORD-19) is an example of a collaborative effort to compile a comprehensive collection of scholarly articles, preprints, and other research output related to COVID-19. By making this dataset freely available to researchers, it facilitated data mining, text analysis, and machine learning research aimed at extracting insights from the vast body of literature on the pandemic.

Personalized medicine: tailoring therapies to individual needs

As data on SARS-CoV-2, from its transmission route to infection mechanisms, accumulated on a massive scale, the question arose of how to turn such a vast amount of data into actionable treatments. Once again, the answer lay in the power of interdisciplinary collaboration to advance patient outcomes. The recognition that there is substantial clinical variability of the disease

stimulated researchers to venture beyond the confines of traditional personalized medicine approaches. This perspective aimed not only to tailor treatments to individual patients but also to identify broader patterns and factors that influence disease severity and treatment response. This stratification allowed for the targeted application of interventions, such as early immunomodulatory agents and antivirals, for those most likely to benefit.

As carefully reported by Cauchemez and colleagues (1), it took only 2 years to develop a wide-ranging pharmacological arsenal against COVID-19. Treatments include highly specific monoclonal antibodies for prevention in immunocompromised patients. Antiretroviral drugs that target SARS-CoV-2 proteases were developed rapidly and approved as early therapeutic interventions in subjects at high risk of developing severe COVID-19. This is a truly remarkable achievement, considering that it took at least 15 years of intense research to identify safe and effective drugs for other infectious diseases, such as HIV.

The example reported by the authors regarding completely new antiviral therapeutics, PROteolysis TArgeting Chimeras (PROTAC) for COVID-19, is also very pertinent (1). This approach aims to degrade pathogenic viral proteins by hijacking the ubiquitin-proteasome system. While this technology is in its infancy, a very recent study reported promising results regarding PROTAC blocking HIV-1 replication through the selective degradation of HIV-1 Nef protein (3).

By combining different types of expertise, personalized medicine holds promise for enhancing therapeutic efficacy and minimizing adverse effects. A clear illustration of the efficacy of this approach in tackling upcoming challenges is exemplified by investigations into long COVID, a frequently debilitating condition that affects at least 10% of individuals following SARS-CoV-2 infection (4). Understanding long COVID poses significant challenges; current diagnostic and treatment modalities are inadequate, necessitating broad collaborations to prioritize clinical trials that investigate the leading hypotheses.

The power of vaccines in ending the pandemic

In their careful examination of the transformations witnessed throughout the COVID-19 pandemic, the authors did not overlook the monumental achievement that was the swift development of safe and effective mRNA vaccines. These innovative vaccines harness the power of mRNA technology to stimulate an immune response against the SARS-CoV-2 virus, offering a potent defense against the global health crisis. As the authors eloquently elucidated (1), these groundbreaking vaccines were not a product of extemporary scientific endeavors but rather represented the culmination of decades of rigorous basic science research in mRNA biology, gene expression, and immunology. Through incremental progress and collaborative efforts across interdisciplinary fields, researchers have laid the groundwork for this transformative breakthrough. This success highlights the critical importance of fostering a robust scientific ecosystem, characterized by sustained funding, collaborative partnerships, and a commitment to evidence-based inquiry.

But the fast development of safe and effective vaccines is not the only achievement to have emerged from the pandemic. These novel tools have encouraged researchers in the field of immunology to expand our understanding of the mechanisms within the immune system that were previously unexplored. Vaccinology has traditionally been an empirical science, focusing on the efficacy of vaccines rather than on the underlying mechanisms. With the advent of COVID-19 vaccinations, researchers are now investigating the intricate cellular mechanisms governing a vaccine's ability to confer limited or long-lasting protection.

Unprecedented numbers of studies and datasets have been published, shedding light on the immunological effects of various dosing intervals and on the administration of both homologous and heterologous vaccines. Researchers have conducted clinical trials and laboratory studies to examine how these vaccines stimulate the immune system and whether they elicit different types or levels of immune responses. Similarly, there has been a surge in research exploring the phenomenon of hybrid immunity and the impact of multiple infections with different viral variants. Lastly, intense attention has been paid to specific groups of people, such as immunosuppressed patients, transplant recipients, and those affected by cancer. This has made it possible to identify finely tailored strategies to maximize the protective effect of vaccines on individuals in these groups.

Advances in omics-based technologies and systems biology have also offered unprecedented opportunities for researchers to scrutinize the effects of vaccination at the cellular level. A transcriptional atlas of the human immune response, for example, has been provided for the first time to predict vaccine-induced responses to 13 different vaccine types (5). This newfound understanding has paved the way for the exploration of uncharted territories in vaccine research and underscores the importance of comprehensive immunological investigations in vaccine development.

All these detailed studies on the immunity induced by COVID-19 vaccines have led to a reassessment of the role of various compartments of the cellular response, such as T cells, which were typically thought to be less involved in conferring protection than B cells, which mediate the humoral response. The importance of these discoveries is exemplified by the emergence of new vaccine platforms that enable the development of robust T cell-mediated responses (6). These advancements have the potential to revolutionize vaccine strategies for a wide range of infectious diseases that currently lack effective vaccines, such as HIV, West Nile virus, and hepatitis C virus.

Building upon this momentum, the insights gained from combating COVID-19 will be pivotal for inspiring novel approaches to address pressing global health threats. While the road ahead may present us with formidable obstacles, by utilizing the knowledge, technologies, and collaborative frameworks established during the pandemic response, researchers may be better equipped to devise innovative solutions and interventions against pathogens that we have thus far been unable to defeat. The example Cauchemez et al. provide regarding antibiotic resistance is particularly apt (1). The efforts made in these last 4 years must be scaled up, sustained, and used not only to address future pandemics but also to deal with the significant threat posed by antimicrobial resistance to identify new and effective therapeutic interventions.

Coupling data and computational analytics to transform healthcare delivery

The pandemic has also highlighted the role of advanced computational analytics and artificial intelligence as invaluable tools for integrating diverse datasets, combining epidemiological trends, clinical phenotypes, genomics, and microbiome profiles into a cohesive framework. The emergence of a "systems medicine" approach, enabled by these technologies, holds the potential to revolutionize disease management by offering a holistic understanding of health and disease.

The rapid adoption of digital health technologies during the pandemic, including telehealth and digital therapeutics, has reshaped healthcare delivery paradigms. These innovations have not only bolstered health system resilience in the face of disruptions but have also expanded access to care and improved patient outcomes.

Looking ahead, while we are still at the beginning of this transformation, the integration of digital solutions into routine clinical practice will be instrumental in implementing patient-centered care and optimizing resource allocation in healthcare systems.

Embracing changes for a healthier future

As we navigate the complexities of the post-COVID era, it is imperative to foster multidisciplinary collaborations that transcend traditional boundaries, encompassing molecular, clinical, and social determinants of health. The article by Cauchemez and colleagues (1) is very welcome, as it provides an extremely detailed overview of the path we have taken and guidance on the necessary steps to continue in this direction. By embracing open science, forging innovative partnerships, and centering patients in healthcare delivery, we can exploit the full potential of advances in medicine to improve public health outcomes and enhance the wellbeing of communities worldwide. This very timely article can be used as a statement of intent and a testament to the resilience and adaptability of science for future generations in order to comprehensively address the most immediate public health challenges.

Statements

Author contributions

LP: Writing – original draft, Writing – review & editing. GR: Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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