Clinical laboratories and pandemics: new and emerging challenges

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The coronavirus disease 2019 (COVID-19) pandemic is not over yet. Although the emergency phase of COVID-19 might have passed, this unprecedented disgrace is still fresh in the minds of scientists, policymakers and general public. We have all experienced extraordinary few years that none of us would like to experience again. The pandemic has impacted all aspects of society, dramatically changing our day-to-day lives and habits, and forcing us to become "experts" in virology, learning terms such as droplets, swabs, lockdown, contact tracing and social distancing. It has also disrupted clinical practice, including many practices of clinical laboratories (1).

An impressive number of scientific papers has been published during the past three years: as the early research tried to make sense of the immediate effects of the virus on patients, healthcare and society, we are now in a prominent position to take a somehow more thoughtful view of the effects of this ongoing pandemic. These reflections include contributions to rethink at what has happened, and is still happening, and to learn essential lessons for the future of our lives, of medicine, in particular laboratory medicine and its professionals (1).

The first question is about pandemics, or better if COVID-19 was an extraordinary and unique event, or whether other pandemics should be considered as possible, probable or certain occurrences. In a recent interview, Erik A. Karlsson, an eminent virologist working at the Institut Pasteur, Centre National de la Recherche Scientifique, Paris, in France, was asked to answer a frequently debated issue during the COVID-19 pandemic, that is *"can we prevent pandemics?"*. His answer deserves much concern, as he replied *"I think we can be better prepared for the next one, that's for sure"* (2). More outbreaks of infectious disease seem to be almost unavoidable due to many environmental and human factors (overpopulation, irreversible climate changes, disruption of wildlife habitats, virus manipulation and so forth), but stopping many of these before turning into pandemics seems a feasible enterprise. The past 20 years of outbreaks, not only COVID-19, but also Zika, Ebola, swine flu, Middle Eastern respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS), can teach us how to improve global health security. Preparing for future pandemics involves strengthening the entire chain of the outbreak response, from identifying the pathogen, through isolation and management of the outbreak, up to mass vaccination (3).

In the paper published in this issue of Biochimica Clinica, Giuseppe Lippi highlights some important achievements of laboratory medicine during the pandemic and provides new perspectives for future strategies to cope with new and emerging challenges (4).

The first lesson is that laboratory tests cannot be evaluated only on the basis of metrological and analytical issues. In particular, all gold standards, including molecular tests such as SARS-CoV-2 RNA RT-PCR, should be used in clinical practice taking into consideration diagnostic accuracy, but also their availability, feasibility, acceptability, turnaround-time, costs and, in such case, relationship with real infectivity should be contemplated. An increasing body of evidence has been collected in the last months to demonstrate that prolonged RNA detection in nasopharyngeal swabs taken from COVID-19 patients does not necessarily reflects an increased risk of SARS-CoV-2 transmission, since the last period of viral RNA shedding is almost sustained by extra-viral genetic material and/or non-vital particles (5). In addition, some concerns regarding the lower sensitivity of SARS-CoV-2 antigen testing could be overcame by incorporation into validated testing algorithm and using appropriate strategies, including higher test frequency (e.g., every 2-3 days). I would like to cite a crucial statement in the fundamental paper by Mina et al. which represented the rationale for the new strategy of laboratory testing during the pandemic, based on adoption of antigen-based assays, shifting our attention *"from a narrow focus on the analytic sensitivity of a test (the lower limit of its ability to correctly detect small concentrations of molecules in a sample) to the more relevant measure of a testing regimen's sensitivity to detect infections (the probability that infected persons learn they are infected in time to be filtered out of the population and prevent spread to others)"* (5). The same authors added a further paragraph that should be a lesson for any laboratory professional "*Clinical tests are designed for use with symptomatic people, do not need to be low-cost, and require high analytic sensitivity to return a definitive clinical diagnosis given a single opportunity to test. In contrast, tests used in effective surveillance regimens intended to reduce the population prevalence of a respiratory virus need to return results quickly to limit asymptomatic spread and should be sufficiently inexpensive and easy to execute to*

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allow frequent testing — multiple times per week" (5).

The second lesson is that laboratory testing cannot be only performed in centralized laboratories, as point-of-care testing (POCT) and home-testing are increasingly needed to improve acceptability, fast, easy and even cheaper access to laboratory information. Moving from the first wave (centralized testing in clinical laboratories) to the second wave (antigen-based tests in decentralized facilities) to the last waves (self-collected samples and self-testing), the role of laboratory professionals needs to change to address the quality of centralized and decentralized results, the integration of different sources of laboratory data and their appropriate interpretation and utilization.

The third lesson is that resurgence of simultaneous infectious diseases, namely new variants of SARS-CoV-2, Influenza, Respiratory Syncytial Virus (RSV), which may be responsible of the "tripledemic", may request innovative strategies based on the use of combined antigen-based rapid tests (Ag-RDT) that would need to be conducted in both centralized and decentralized settings, in symptomatic patients as well as in vulnerable persons, before hospital admission and in whatever other circumstances associated with higher likelihood of contagion.

I sincerely invite all the interested colleagues to a careful reading of the article written by Giuseppe Lippi (4), which deserves merits and may explain the reason why the European Federation of Laboratory Medicine (EFLM) has recently decided to establish a new functional unit on "Preparation of Labs for Emergencies", appointing Professor Lippi as chair of this new and strategic project.

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