Life With SARS-CoV-2/COVID-19

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The "next big pandemic" is happening now. It was expected by scientists who warned the governments and politicians around the world but were ignored because they were too busy cutting the budget for the health systems and scientific research in favor of other affairs.

The alarm of scientists has been disregarded repeatedly. By ignoring our history (which teaches us many things-- social distance and the use of masks, currently, are the only forced and effective resources that we managed to field and are exactly the same as 100 years ago with the "Spanish" flu pandemic), we are left vulnerable despite several scientists who are studying on shortening the period of this pandemic that brought health, social and economic crises.

The transition from the pandemic to the endemic containment phase is complex and will require a multitude of citizens to resolve the situation. The development and distribution of vaccines are now close but we must still be cautious. In this article, an analysis of the situation, particularly in Italy, will be made.

Keywords: SARS-CoV-2, COVID-19, pandemic, spillover, development model, ecosystem, economic crisis, epidemiology

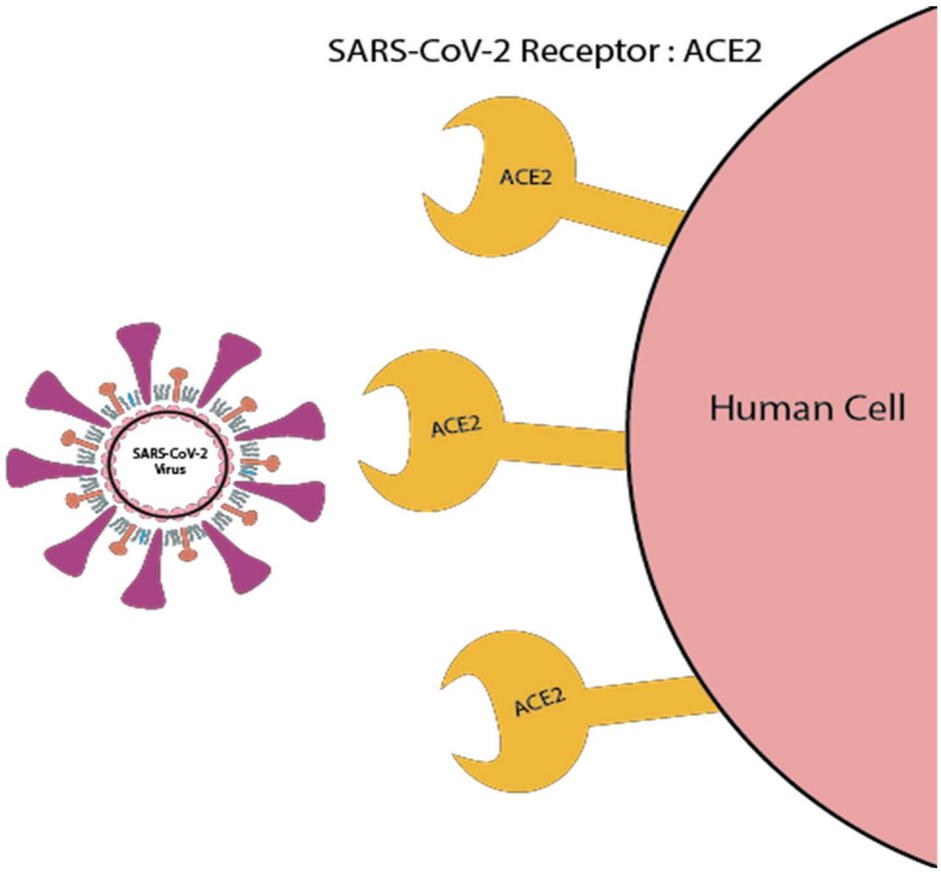
INTRODUCTION

Around the world, the most complex moment in the choice of the possible ways to manage the current health and economic crisis is the transition from *lockdown* to the long phase of coexistence with SARS-CoV-2/COVID-19, having - specifically - at present, an absence of certain treatments (antivirals proven to work adequately and specifically for the treatment of the pathology by this new virus, monoclonal antibodies, etc.) and vaccines (several of which will enter, in the coming months, the clinical trials phase, some of which, as recently announced, will be tested directly and dangerously on humans, omitting the pre-clinical animal trials phase, usually carried out on rodents or other small mammals).

In the mean time, I present a very brief commentary on the lockdown in progress and completed, at different times, in Italy, for nearly two months. It did not work magnificently in Italy, it is evident. On the other hand, we were, with merit, the first in the West to apply it, but we also admitted, from the beginning, that we are not China or even Taiwan or South Korea where the number of infections, apart from some outbreaks, has remained almost unchanged. So much so that China, with its approximately 88,000 cases, has quickly fallen in the grim ranking of countries with the most widespread infection rates (far behind the United States, Brazil, India, Russia, South Africa, Mexico, Peru, Chile, Colombia, Iran, the United

Kingdom, Spain, Italy, France, Germany, etc.), while Taiwan and Korea, despite being among the first countries where the virus spread, remain at the bottom of the list.

FIGURE 1
REPRESENTATION OF SARS-COV 2 VIRUS AND RECEPTORS



Why did the lockdown in Italy work poorly and so slowly for some areas such as Lombardy? My personal idea is that it is due, in part, to the delay with which it was imposed at the national level throughout the territory and in large part, also, to the constant pressure of the General Confederation of Italian Industry (Confindustria) which, unable to consider that the problem is generated and established within the capitalist system of production (of the history of spillovers, increasingly frequent and "stimulated" by human pressure on ecosystems - and therefore on the planet - enough has been said[1]!), has ensured that more than 40% of Italian industries, including those related to non-essential goods, continue to operate during lockdown with simple safety adjustments, sometimes complex or impossible to realistically apply in the production chains. Even the FIOM, which compared its own data with that of the ISTAT, tells us that in Lombardy, during lockdown, there were over 450 thousand companies in operation out of a total of about 800 thousand[2]. Obviously, an accomplice was the Government which, despite the pathos of the Prime Minister, Giuseppe Conte, turned a blind eye following the wishes of the industrialists, enriching the list of activities excluded from the "lockdown", many of which the international capital system does not want to stop even during a pandemic!

That said, analysis of official data on the evolution of the pandemic in Italy shows that, before the number of cases dropped sharply in July 2020, it was on what the ISS called the "plateau", a very long and enduring one, with many hundreds of deaths per day and thousands of new infections, despite initially reaching the important and fundamental objective, of reducing the R0 factor (which became Rt when the

containment measures were adopted) below level 1, that is, immediately after the lockdown the R0 factor which was initially estimated at almost 3 (each positive person was capable of infecting 3), fell below 1 after the adoption of the containment measures. However, at the time of writing, in early August 2020, there are still several hundred new infections per day. We are now in the middle of summer, in Italy the end of the widespread lockdown dates back to May 3rd, and in the following days there have been progressive partial openings. The situation to date appears to be that of an endemization of the pandemic in Italy with some 250 thousand confirmed cases of infection and almost 1.5 million cases of infection estimated through a sample of 64 thousand serological tests carried out to date.

I imagine the future, at least for a year, as a bellows, a kind of accordion, with partial openings followed (as soon as the outbreaks reappear) by total closures. At least until the production of the vaccine and the beginning of related large-scale vaccination campaigns and/or the progressive and slow, but natural achievement of herd immunity. In short, a year, maybe two.

The transition from the pandemic phase to the endemic containment phase is as complex as it is not easily predictable and will evolve in direct proportion to the steadiness and active action in which everyone, as a multitude of citizens in the life of the country, each with his or her own role, becomes involved. Until now, lockdown has mainly provided for a passive action by everyone: to stay home. The only exceptions have been represented by the weekly moment of grocery shopping or by the quick excursions to the pharmacies or parapharmacies for those who needed it, or even by the short, allowed, necessary and harmless walks around our own house, despite the mediocre denouncers who act according to the "perfect subject formula"[3].

In contrast, we must get used to actions that are able to make us return not to normality (it is impossible, in the short term, in the strict sense) but to a coexistence between human beings who interact with each other, possibly in collaboration and at the same time vigilant towards the virus, perhaps without losing sight of the humanity that will have to be the figure to continue a life together that is compatible with the solution of daily problems. The actions of the governments (obviously I am interested, in this sense, in what the Italian government is doing or intends to do as a continuation of the management of the crisis) will have to be increasingly prepared to provide the efficacy that, until now, frankly, has been very limited if we think only of the economic measures and the general delays accumulated until now, to cope with the daily difficulties, for tens of millions of people. It is clear that democratic and effective action by the Government is of fundamental importance to continue the management of the necessary long-term coexistence with the virus, so as not to run into complex problems of anticipation and dimensioning if the response to the growing social and economic difficulties continues to be as suffocating and insufficient as it has been up to now. On the other hand, as recently stated by Frank Snowden[4], professor at Yale University, historian of epidemics and medicine, pandemics have the potential to reinforce authoritarianism (as is happening in some Eastern European countries) or, on the contrary, to favor the liberation movements of the people as with the "*end of slavery in the plantations of Haiti, for example, which was the result of the destruction of Napoleon's army due to yellow fever. And that was liberating: the first free Black Republic, the first great slave rebellion in history, based in part on the difference in immunity and mortality between Europeans and Africans, Napoleon's troops, the Europeans, had no herd immunity against yellow fever, while the African slaves did*".

From the technical-scientific standpoint, this is unfolding in several ways, but it has not become as urgent as the start of large-scale campaigns in territories all over Europe and possibly all over the world, perhaps on a regional or provincial basis, to carry out new serological tests in order to understand the real extent of the spread of the disease, since the most plausible hypotheses were initially in the range of 2.5[5] to 6 million[6] Italians allegedly infected and mostly asymptomatic (the sample of 64 thousand Italians examined so far seems quite small, but it is still significant, highlighting, as already mentioned, a minimum of 1.5 million citizens who have developed antibodies), thus far exceeding the less than 250 thousand, so far, formally detected with pharyngeal swabs. This would modify the lethality rate to about 2%.

This requires a very effective strategy that is widely chosen by the scientific community and is not the prerogative of a small group of scientists and economists (a working group perhaps too unbalanced in favor of a liberal vision). Recently, a working group of 150 Italian academics[7] has been assembled through which seven concrete requests have been made to the Government to gradually reopen Italy, starting with the

"*progressive adoption of alternative measures to the widespread use of isolation at home*" and the use of "*contact tracing of transmission*" strategies.

The Executive is urgently demanded "*a representative sample of the population to understand the real extent of infection and the lethality of the virus*" and "*the progressive adoption of alternative measures to the widespread home isolation, as part of a clear strategy to contain the spread of the virus*".

Specifically, "*the use of contact tracing of transmission*", "*the early identification of positives through mass molecular and serological testing*", as well as "*the start of large-scale production of the material required for molecular and serological testing*" is demanded.

Roughly of the same opinion is Guido Silvestri, professor and head of the Department of Pathology at Emory University in Atlanta, director of the Division of Microbiology and Immunology at the National Primate Research Center in Yerkes, and a member of the Emory Vaccine Center, who in a message, signed by other Italian academics, sent to the relevant authorities and spread to the public through Facebook, says:

> "*To gradually return to our normal life, we propose the creation of a flexible monitoring and response body, FMR (MRF in Italian), for SARS-CoV-2 infection and the resulting disease (COVID-19) and possibly, in the future, for other epidemics. This new body, with clear regional articulations, which we plan to operate under the coordination of Civil Protection (PC) and the Ministry of Health (MinSan) and the technical support of the Instituto Superior de Sanidad (Higher Institute of Health)(ISS), should have the following general characteristics:*
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> *i. resources and capacity to carry out a very high number of tests (at least in the order of many thousands per week) both virological and serological in the general asymptomatic population, with very rapid authorization procedures by the central government and the various regional governments to be used in case of signs of activation of new epidemic outbreaks;*
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> *ii. an improved central surveillance structure in the ISS, responsible for both the analysis of quasi-real time data and their regular submission by the Ministry of Health directly to the Government, Parliament and supranational health bodies;*
>
> *iii. the strengthening of regional capacity for epidemiological surveillance through peripheral monitoring centers distributed throughout the territory and with the development of epidemic intelligence systems that detect any sign of an outbreak at an early stage;*
>
> *iv. the strengthening of the network between the operational structures and the professionals who constitute the first line of interception and defense against SARS-CoV-2/COVID-19 in the symptomatic phase of the pathology, promoting the integration of the network of infectious diseases widely spread in the Italian territory with that of general and territorial medicine, with a hubs & spokes approach of the same level;*
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> *v. legal mandate to propose in a timely and possibly binding manner flexible measures in response to signs of viral resurgence, including forms of social isolation (suspension of activities, sporting events, schools, etc.); case investigation of infected persons and contacts (applied also through the use of appropriate technologies such as smart phones, applications, etc., as already tested in Singapore and Korea), strengthening of specific health facilities; sharing the communication strategy with the Order of Journalists and the main national newspapers, as well as with the main public and private radio and television stations, in order to avoid the potential damage of both exaggerated alarmism and simplistic or even denialist underestimation (also taking advantage of expertise in the doctor-patient relationship field).*

We are aware, of course, that such an ambitious, strictly data-driven, organic project of flexible monitoring and response (MRF) to the risk of reactivation of SARS-CoV-2 infection represents a significant investment of resources, necessary for its rapid implementation in the next four to six months (personnel, infrastructure, testing, analysis, etc.).

Similarly, we are aware that the creation of this "MRF" body will require the detailed definition of a regulatory perimeter within which to operate, as far as possible, in harmony and synergy with the relevant political, administrative, health, and technical-scientific entities, both at the national and local-regional levels.

The strengthening of the health surveillance and response system should be accompanied by a general plan to limit the risk of activation of epidemic outbreaks in the workplace and in the education system. This plan should include a major restructuring of procedures and activities that will have to be redesigned to limit the spread of respiratory viruses.

Although a detailed economic and regulatory evaluation of the current project is beyond the scope of this first presentation of the proposal, we believe, however, that it may be a reasonable path, from the epidemiological and virological point of view, for the return to normality, during the forced period of coexistence with the coronavirus that -we hope- will be interrupted as soon as possible with the arrival of a vaccine".

I chose to give an exhaustive report on Prof. Silvestri et al.'s proposal because it seems quite clear to me that if we don't start, from the beginning, to properly communicate what and how the phase that the government has defined as "phase 2" will be, we run the risk of wasting time and going backwards, dangerously giving back strength and space to the virus.

In fact, it will be fundamental to communicate very clearly what from May, with flattened curves, we will all do together, it will be fundamental in the medium and long term to attain safe treatment (antivirals and/or combination of other drugs) and massive immunization (favored by the vaccine as well as the spread of antibodies in the subjects who have contracted the virus).

If we go back to reflect about the virus, it is worth remembering, once again, that this living acellular form can replicate itself only and exclusively in a living cell, that is, it has an extreme need of those who transport it continuously in the sea of life, it is an obligate intracellular parasite, it depends totally on others; to live it depends on replication mechanisms provided by hosts because it is not able to replicate itself in an autonomous way. Basically, we should not be mistaken when, little by little, we Italians, but little by little all the others too, will have to emerge from the lockdown. This non-organism, barely a few millionths of a millimeter in size, has only one purpose: to pass from one host to another in order to continue to replicate very quickly (a common characteristic, speed, of all single-stranded RNA viruses) and continue - therefore - to survive. In fact, it is precisely through mutation, an essential mode of genetic variation on which natural selection acts, that the very survival of the virus is guaranteed. Mutations can usually be adaptive or harmful and, in the latter case, can lead viruses to what biologists call an evolutionary dead end. However, the enormous number of mutations can, probabilistically, make some of these mutations beneficial and, therefore, useful from the point of view of adaptation. This seems to have happened with SARS-CoV-2, since its adaptation not only culminated in its spillover from an animal reservoir (one of the different species of bats) into *Homo sapiens sapiens*, but in the latter it found an easy vehicle to pass from one individual to another, thanks to the enormous number of individuals of the human species and their great capacity of contact and, therefore, of transmission. It is also true, on the contrary, that there is a possible upper limit to the rate of mutations because the greater the number of them, the greater the possibility that, sooner or later, a lethal mutation will occur. I wonder at this point, but this question should be posed to virologists and epidemiologists, whether the temporary confinement of the virus through social isolation with the direct benefits that we already know (in terms of reducing deaths and, more generally, reducing the impact on health systems that are woefully unprepared for the pandemics widely expected and

announced by the WHO), prevents in the long term, the realization of this possibility of freely giving the virus the "option" to fail by going through a dead end, for the sake of humanity that lives this burden with anguish and legitimate concern.

It is precisely this unpredictable mutant ability that makes RNA viruses such as SARS-CoV-2 "slippery", so fast that it should not be underestimated or questioned, as mistakenly happened in the last period, for the potential duration of immunity acquired by subjects crossed by the pathogen is doubtful. Such conclusions are based on some reports from China, other Asian countries and Europe, that despite the immunoglobulin G, IgG, the so-called "memory antibodies", there are reports of reinfection in subjects who had already contracted the pathogen. Whether they are real reinfections or false negatives, we will find out soon, but it would be a problem if the virus mutated at such a high rate. However, it may be necessary to wait a few months to give scientists time to fully understand.

In addition, virologist Guido Silvestri points out that it is extremely interesting that in the United States, despite the absence of significant government measures, the infection curve in recent days continues to decrease and follows the forecasts of Levitt and Friston. The virologist's opinion in this regard, in relation to the United States which, together with Brazil, represents the place on the planet with the greatest human disaster caused by the coronavirus, refers to the so-called "immune dark matter" of SARS-CoV-2, which seems to confer immunity to a large part of the population. This concept is a topic that will undoubtedly be studied in the future by virologists and epidemiologists.

A fact that is hardly spoken about is the relationship between a pathogen and its host. It is a relationship that is constantly evolving, a relationship that could be called dynamic, thanks to which, over time, the pathogen can become less virulent and the host even more tolerant. I do not claim this, but the history of epidemics (and pandemics) tells: in the long run, the biological dynamics find a balance between the parasite and the host. It is quite evident that in the case of SARS-CoV-2, being a recent spillover, that is, a recent species jump, we seem to be completely new hosts and therefore in this initial phase (because we are talking about only six/eight months since the virus began to spread according to molecular studies that date the circulating virus to the last quarter of 2019) in which the virulence is being expressed with the strength that we have seen, that is, about 2% of global lethality[8] (the Italian case will presumably be analyzed by extrapolating Lombardy from the general context, because it will be studied specifically). As a way of saying, the virus takes advantage of the host but not too much, because it needs the host to continue to mutate and live, so it damages it but not beyond a certain point, it needs "legs" to continue to walk, to continue to infect and therefore to replicate and mutate. On the other hand, Hans Zinsser, American physician and bacteriologist (who lived between the second half of the 19th century and the first half of the 20th century) said that between a parasite and its host there is a tendency to an evolutionary adaptation that leads to a better mutual tolerance.[9]

We are in the midst of what virologists, for at least two or three decades, have called the "Next Big One".

The "next great pandemic" has arrived, as expected by scientists around the world who had warned governments and politicians that, needless to say, were ignoring everything and everyone because they were too busy cutting back on health systems, public education systems and scientific research in favor of increased spending on weapons and speculative matters of various kinds. At the time of writing, there are as many as 188 of 196 States in the world where the new coronavirus has spread (with almost 20 million infected and about 700,000 deaths in a few months). Perhaps no virus had ever accomplished so much! Although it is estimated that the Spanish flu claimed between 50 and 100 million victims between 1918 and 1920, it did not reach the most remote corners of the planet, probably because one hundred years ago the current capacity of humans to move did not exist. The current virus widespread around the world in just a few weeks through saliva drops (Flügge drops), named after Carl George Friedrich Wilhelm Flügge, a German bacteriologist and hygienist thanks to whom surgical masks were invented at the end of the 19th century. Yes, it is precisely the masks that the Italian government should guarantee and distribute widely (not only and primarily to health care personnel who, not sufficiently guaranteed in this sense, have also been infected!) to the population if it really wants to implement "phase 2" in a lasting way. It is necessary to go beyond the summer of 2020, which concedes benefits at a time when, in Italy, the infection situation

seems to be under control (also thanks to the weakening of the virus by UV rays, as has been scientifically proven recently) with the conscious and active attention of a multitude of citizens willing to return to a "normality" that cannot really be normal until endemization is widespread and verifiable all over the world and until we have effective tools to fight against it and, ultimately, to live with it.

This continued disregard for scientific facts, and the continued lack of attention for the study of historical facts, which also include the recent past that has so much to teach us (social distance and the use of masks are, for the moment, the only forced and effective resources that we have been able to take advantage of and are exactly the same as they were during the "Spanish" pandemic of 100 years ago), makes us very vulnerable, even though today we have a by no means negligible number of scientists who are studying how to shorten the times of this pandemic and how to try to return to normal while we wait for the end of the health crisis, which will not be the end of the social and economic crises. In fact, normality is understood, it should be clarified, not in the sense that we could have understood until a few months ago. I am pleased and I think it is appropriate to quote, in this regard, Pierluigi Sullo, an excellent analyst of what is happening, who, in a recent article, says "*...we must urgently equip ourselves to create a new normality. And for this we need a cultural "spillover", an overflow of ideas and projects and ways of seeing the world outside the forced reservoir in which we have all been locked for forty years, that is, since the expansion of neoliberalism*".

ENDNOTES

1. David Quammen – Spillover – Adelphi 2014
2. Andrea Cegna - *Oltre il lockdown, le aziende lombarde sono già al lavoro (Beyond the lockdown, companies in Lombardy are already working)* - il Manifesto of 14 April 2020.
3. Enrico Dal Buono - *Finalmente i mediocri hanno trovato la loro eccellenza: restare a casa meglio degli altri (Finally the mediocre have found their excellence: to stay home better than others)* - RollingStone, 13 April 2020
4. Stella Levantesi - *L'epidemiologo Snowden: "Questa pandemia specchio di una globalizzazione letale" (El epidemiólogo Snowden: " This pandemic reflects a lethal globalization")* - il Manifesto of 9 April 2020.
5. (https://imperialcollegelondon.github.io/covid19estimates/#/)
6. AA. VV. - *Estimating the number of infections and the impact of non-pharmaceutical interventions on COVID-19 in 11 European countries* - Imperial College COVID-19 Response Team - London, 30 March 2020.
7. AGI-Agenzia Italia of 13 April 2020