

A pandemic foretold (in vain)

A last report

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It is not easy to give a summary of these first 6 long months of pandemic. Our earlier article *The Italian Drama* (Burgio E., 2020) sought to put in context the situation in Italy within the planetary one, which is still evolving. Yet, it is necessary so we do not find ourselves unprepared should the virus return with high viral loads in Italy and the rest of Europe in late summer or autumn. In the terrible days of March and April, the most affected provinces of Northern Italy were Bergamo, Brescia, Cremona, Piacenza. Unfortunately, the virus now rages, in many areas of the planet: United States, Brazil, Mexico, India. To place the pandemic in context, means examining previous events historically and then focusing on recent pandemics. The first big mistake was not understanding that the appearance of a pandemic virus is a dramatic event to be studied according to well-defined coordinates, known for over a century. This was forgotten by many famous and expert scientists.

We had forgotten that pandemics are epochal dramas

Let's start from ancient history. Large pandemics are epochal events that generally followed tragedies: wars, famines, natural disasters. It is important to highlight that these are not random events, but dramatic consequences of great ecological, biological and social imbalances.

Great pandemics such as the Plague of Justinian (540-542 AD), the bubonic plague of the 14th century better known as the Black Death (1346-1353), the great cholera epidemics of the 19th century (1850-1860) and above all the great global endemia due to the most terrible biological killer in human history, Variola major, the Smallpox virus. Alas, we only have confused narrations devoid of scientific value. The chronicles of contemporaries are difficult to derive value on a biological and sanitary level. Yet, it is clear that these all were events that imprinted an indelible mark on collective consciousness.

In the Middle Ages, the bubonic plague of the 14th century, the Black Death epidemic that shocked Europe, undoubtedly left the most dramatic scars. Estimates oscillate between 70 and 200 million deaths, a significant share of the entire human population. Yet these figures fade in comparison with the threat that smallpox presented in the twentieth century. Smallpox could have well taken 200 million lives before it was eradicated through a vaccination campaign that by far is the greatest success of WHO, the World Health Organization.

The great Spanish influenza, prototype of modern pandemics

With the great Spanish Pandemic of 1918-19 we enter the era of modern pandemics, all characterized by a virus that recently made the spillover - a sudden adaptation to man from a reservoir species that has hosted the virus for millennia. During the 20th century, pandemics have always been flu viruses. The first of these was the H1N1/1918, called the Spanish Flu, a dramatically virulent pathogen which emerged from the natural reservoir of flu viruses of migratory birds. During the First World War, American soldiers exported the virus in Europe where it spread like wildfire. It is still remembered as the largest modern pandemic. After killing several hundred thousand people in early 1918, the virus seemed to decrease during the summer, but returned in a much more virulent form in the autumn and the deaths numbered tens of millions in a few months. Shockingly, these pandemic deaths were four times higher than those of the Great War, in much less time.

It is also important to remember that H1N1 has remained endemic in the human species since then. It was replaced in 1957 by the H2N2 of Asian flu and in 1968 by the H3N2 of Hong Kong flu. It seems to have re-emerged from a Russian laboratory in the 70s, in form fortunately not very lethal and since then, together with H3N2, it circulates the globe causing seasonal epidemics, usually not particularly violent, nonetheless causing tens of thousands of deaths worldwide every year.

In recent history, we must remember that from 1997 to 2005 various subtypes of flu viruses made the feared spillover - from migrant and sedentary birds to man, leading to hundreds of deaths. They alarmed virologists because of their high virulence but were not very contagious since these viruses did not acquire the mutations necessary to engage the human respiratory tract. Unfortunately, the new SARS-CoV-2 managed to acquire these mutations in a few months, probably in the autumn of last year, in the province of Hubei in China.

The early warnings during those years, concerning a possible new flu virus pandemic, had two effects: on the one hand, they led to the deepening of research in this area relatively neglected for decades; on the other hand, they generated in many the erroneous belief that they were "false alarms". A fact that would be decisive for the confusion that has recently arisen in this field.

The "new kingdom": Coronavirus and bats

Simultaneously with the avian flu alarms, a new Coronavirus appeared in China in 2002, capable of causing lethal pneumonia in hundreds of subjects, essentially doctors and nurses. It was called SARS (acronym for Severe Acute Respiratory Syndrome). In this case, there was a pandemic early warning, but fortunately the virus proved unstable and was unable to transform itself into a true pandemic, despite being very contagious and virulent.

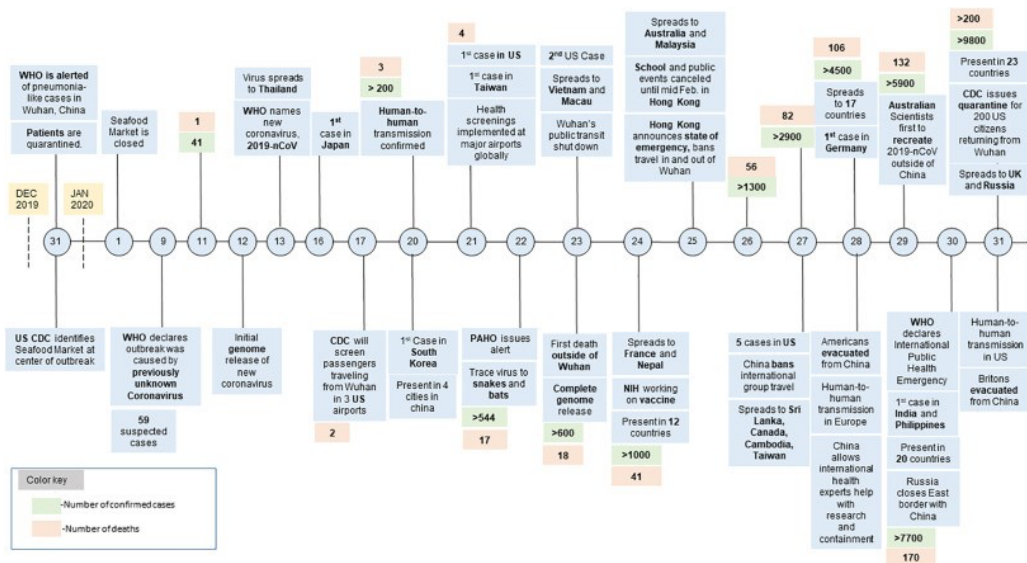
Since then, these Coronaviruses, coming from a new reservoir species, the bat, have been the subject of many studies, because the bat represents for many reasons a much more dangerous reservoir species than the avian populations, which have been the reservoir of influenza viruses for millennia, essentially for two reasons. First of all, because the bat is a mammal, much closer to us on the phylogenetic level. This makes the evolutionary adaptation of its viruses easier to the receptors of our airways and their ability to spread in our species and attack it (that is, to make the fateful spillover). Secondly, because, of the serious eco-systemic and urban alterations caused by man in recent decades, the large bats typical of Southeast Asia now live in close contact with the inhabitants of the large urban suburbs and this makes it much easier to exchange viruses with other animal species and the events of genetic recombination between different viral strains, which facilitate their adaptive evolution.

A pandemic announced long ago and in vain

At this point, we must emphasize that the current one is a long-announced pandemic: first of all because the first SARS, that of 2002-2003, was immediately recognized as a dangerous episode, because of the emergence of a new Coronavirus, totally unknown to our immunocompetent system, and therefore potentially pandemic. Ten years later, in 2012, a second Coronavirus caused an epidemic of small size, but equally dangerous, given the high lethality of the new bat-Coronavirus, MERS-CoV. Finally, in recent years the "virus hunters" have discovered in the caves of Yunnan, China, numerous bat-Coronaviruses, very similar to that of SARS, capable of infecting humans (Qyu, 2020). As a result, many experiments aimed at genetically modifying these viruses to better study their infectious and pathogenic potential and, inevitably, violent criticisms and requests for a moratorium against these objectively dangerous researches followed (Butler, 2015). This became a complex problem because a hypothetical moratorium could be applied only to research conducted in the main laboratories (with safety and international controls), but not to any genetic manipulation conducted in far less safe and uncontrolled laboratories. Because of this, the entire community of scientists in this field has been asking for years to prepare for the worst. Yet, as we will see, only the Asian countries -- which in the last two decades had faced the pre-pandemic alarms related to avian flu and SARS -- adequately prepared themselves to face the emergency, while the Western countries generally found themselves completely unprepared for the foretold pandemic.

First phase: the Asian countries show to be prepared

Now we can try to better understand the trajectory taken by the new virus in the first months of its spread among human beings and to take stock of the pandemic in progress. A quick glance at a chronological plot concerning the most salient events of the very first pandemic phase Fig. 1 offers important data.



Arguably, the Chinese had understood at least since the beginning of December 2019 what was going on. However, the first official reports about pneumonia cases likely associated with a new Coronavirus and the first restrictive measures did not arrive in the West until the end of 2019.

On December 31st, CDC and WHO launched an early warning, about some suspicious cases, outgoing a food market near the city of Wuhan in the Hubei region. On January 9, WHO stated that (as feared) a new Coronavirus was spreading and the Chinese scientists published the entire genetic sequence of it on January 12 (XinuanNet, 2020), soon followed by the Institut Pasteur (Pasteur Institute, 2020) and other prestigious laboratories all over the world (Doherty Institute, 2020).

In a few days, some cases of pneumonia due to the new Coronavirus, initially called 2019-nCoV, were reported in Thailand and then in Japan, South Korea, Taiwan. The media around the world began to spread dramatic stories and alarming images. The Chinese created in record time alternative health corridors and new hospitals solely for diagnosing, monitoring and isolating cases. Meanwhile, other Asian countries were also preparing for the worst. Within days, the virus appeared not only in Hong Kong, Cambodia and Sri Lanka, but also in Nepal and then in France, Germany, Canada and Australia. This was completely predictable, given that in 2020 a pandemic virus travels on transcontinental flights and can easily spread in the world in 48 hours.

It is still difficult to understand why Western countries underestimated these events.

Western countries underestimate the problem

In Italy, on January 31st, the announcement of the dangerous outbreak appeared in the *Gazzetta Ufficiale della Repubblica*. All Italian regions were invited to prepare for a possible pandemic. In fact, three weeks would pass before the first containment countermeasures were put in place, both from the WHO (which only in March would have declared the pandemic alarm), and from infectious disease specialists, pulmonologists and other experts, who tended to reassure that the health systems of the Western countries could face a health emergency such as the one expected (which prove unfounded).

The political leaders of some countries, in particular Anglo-Americans, even declared that it would make no sense to implement containment strategies such as those put in place by Asian countries, that would slow down and damage their economies. This erroneous belief that it would remain an epidemic like many others,

caused a certain number of deaths among the most fragile and elderly, but allowed it to spread across the developed countries.

These were incorrect predictions. The virus would essentially spread in Western countries and in the most economically developed areas, hitting the strata of these societies that travel more and have more direct relationships in closed and crowded places, where the infection spreads more easily.

Italy was the first of the Western countries to be hit, especially in the rich regions of the North and precisely in the most advanced industrial and commercial areas, connected with the rest of the world and more polluted. On February 21-22, the first two outbreaks were discovered in Veneto and Lombardy: the completely different reaction by the political-health institutions of the two regions had significant and potentially illuminating consequences. The Veneto region rapidly put in place, starting from the so-called "red zone", a series of containment and monitoring strategies for symptomatic cases and their contacts, closing schools and universities, blocking the Venice Carnival. These actions reduced the spread of the virus and the number of deaths. In Lombardy, on the contrary, for over a week it was decided not to put in place restrictive measures, which allowed the virus to spread during major sporting events and to invade the hospitals and the nursing homes for the elderly. The consequences were catastrophic. As of July 15, Lombardy has about half of the deaths of the entire country (16,790 declared, but over 18,000 estimated on 35,000 total) and is the region that finds it hardest to contain the chain of infections. A clear demonstration that the first days are the most important to contain a pandemic, because if the containment measures are not implemented immediately, the inevitable exponential curve of the infections and deaths soon reaches considerable numbers and maintains them.

The month of March was the most dramatic one in Italy (Burgio, 2020). While drastic containment and monitoring countermeasures in Asian countries blocked the spread of the virus in a few months, Europe became the new epicenter of the pandemic and the underestimation of the alarm (finally formalized by WHO) was immediately evident. Neither diagnostic tools, nor monitoring plans, nor protective devices for health workers, nor even alternative health corridors had been put in place.

In China, Korea, Japan and especially in Vietnam and Cambodia, the number of cases and deaths within a few weeks began to drop dramatically and rapidly ceased. After all, only in China the situation had been initially dramatic with 90,000 confirmed cases and 3,500 deaths in the Hubei region alone. In Japan and Korea a few dozen deaths were announced, while in Cambodia and Vietnam in the face of a few dozen cases there had been no deaths. These data remain almost unchanged after months, confirming the rule concerning the importance of containment measures.

Initial errors: the epidemiological-clinical framework

Meanwhile, the first reliable clinical data arrived about the initial outbreak and the real behaviour of the virus. Between February 16 and 24, WHO had sent a commission of experts to five Chinese regions (Beijing, Wuhan/Hubei, Shenzhen, Guangzhou and Chengdu). A detailed report was quickly published and for a long time, for better or for worse, it was the basic document for facing the pandemic.

For better, because it demonstrated the immediate effects of the lockdown and other monitoring and safety countermeasures of the health areas, confirming what is the golden standard in the event of a pandemic:

1. to isolate and trace not only symptomatic cases, but also their contacts, to stop it immediately on the territory, without letting the virus spread to the health facilities;
2. informing and involving ordinary citizens, who, for previous experiences (avian and SARS alarms) immediately showed to be aware of the risks and very responsible.

For worse, the underestimation of the number and the role of asymptomatics favored the spread of the virus. This was a fundamental error. In over half of the cases, the virus is potentially contagious with asymptomatic or paucisymptomatic cases.

It is difficult to evaluate the medium- or long-term negative effects of these initial errors. We can certainly hypothesize that if the Western countries had recognized the need and effectiveness of rapid

countermeasures, the first pandemic phase would not have had the dramatic trend we are experiencing now. It is true that if we limit ourselves to testing the full-blown cases, characterized by prolonged fever, severe asthenia, cardiovascular, neurological and respiratory symptoms, we will ignore the dissemination of the virus which occurs essentially through asymptomatic and paucisymptomatic subjects. But even if it were true (as some argue) that the Chinese underlining the large number of a-symptomatic cases would have led WHO experts to underestimate the contagiousness and the danger of the new virus, it must be recognized that none of the Asian countries made the mistake of reserving diagnostic tests for full-blown cases.

It is therefore probable that this huge mistake by Western countries was a consequence of the unpreparedness.

1. The shortage of the diagnostic tools and protective devices for health workers.
2. The inefficiency or even the absence of tracking and monitoring systems.
3. The failure to activate alternative access strips and dedicated health areas.
4. Hospitals and health care homes for the elderly transformed into "sanctuaries" of the virus.

All these fundamental problems are still unsolved in many Western countries.

The Chinese divide and the global divide

To understand the importance of putting in place rapid and effective containment strategies and, above all, to demonstrate how much initial errors can affect the pandemic trend, it is sufficient to quickly consider the totally different evolution of the pandemic in the different areas of the world. First of all, it is useful to remember that Chinese epidemiological data immediately confirmed the great effectiveness of the correct containment and tracing strategies: most of the cases and deaths occurred in the Hubei region alone, immediately isolated from the lockdown. Similarly, mortality rates were 4.5% in Hubei and <1% in the rest of the country.¹ (Fig. 2)

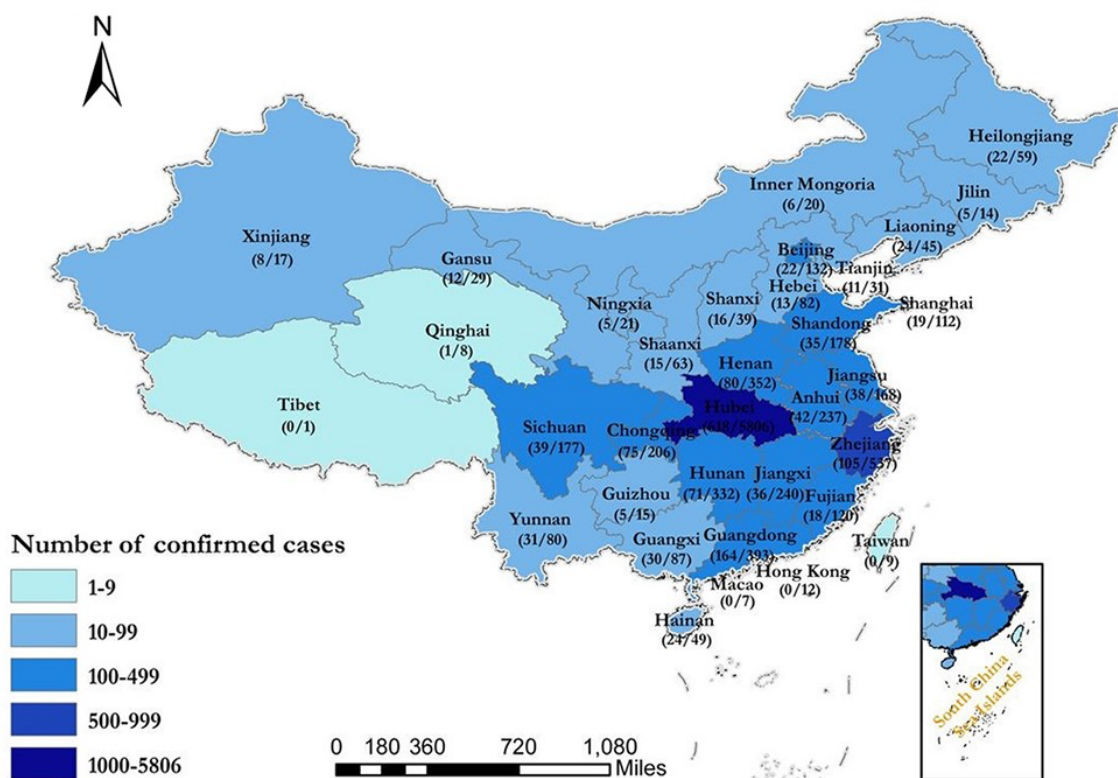


Fig. 2. The Chinese "divide": clinical features and outcomes of patients hospitalized with COVID-19 in Hubei (epicenter) and in the rest of the country. (China European Respiratory Journal, 2020; DOI: 10.1183 / 13993003.00562 -2020).

As a demonstration that only the countries and regions that have been able to rapidly implement effective containment measures were able to interrupt the chains of contagions, by reducing in a short time the virus circulation and the number of subjects with high viral load, is sufficient to give a quick look at two graphs relating to the different trends of the first pandemic phase in Asian countries compared to Western ones (Fig. 3)² and in the regions of Northern Italy with respect to the Center South of the country (Fig. 4)³.

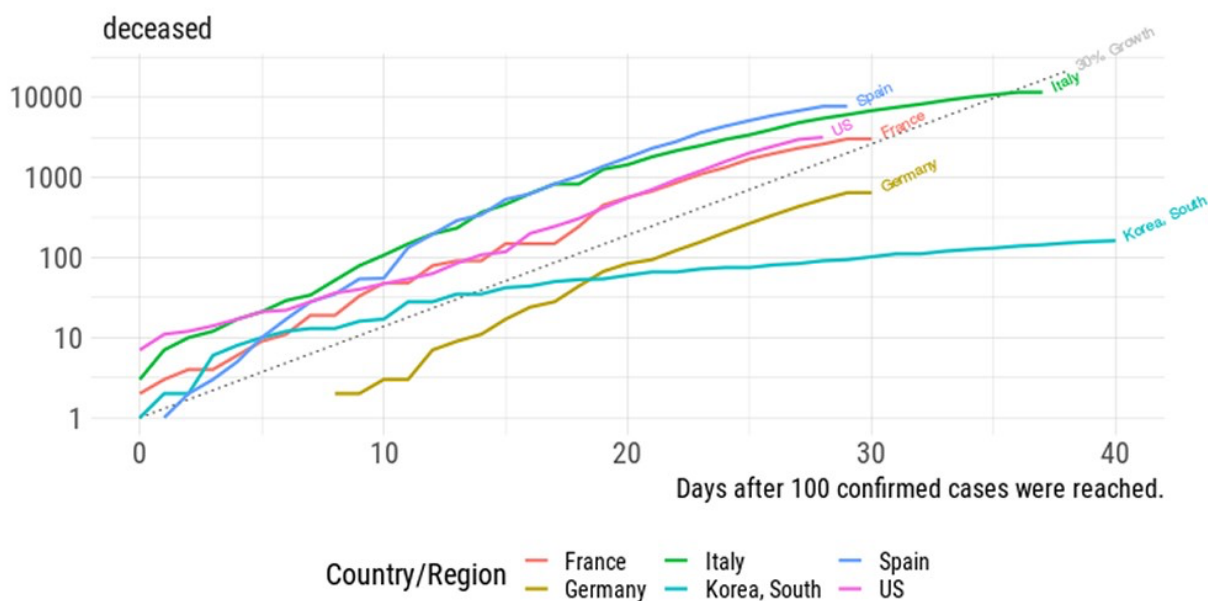


Fig 3. The "global divide": Asian versus Western countries. The different patterns of increase in the number of deaths for COVID-19 are outlined. The cumulative number of deceased is considered from the first day with 100 recognized cases. South Korea is taken as an example of an Asian country, accustomed to managing this type of emergency and "vaccinated" by pandemic alarms related to avian flu outbreaks and SARS.

As for Italy, a similar epidemic divide was immediately evident between the Northern and Southern regions. In the Southern regions that were able to benefit from a much longer latency time (North-South gradient) the lower circulation of the virus and the low viral load in the infected subjects made the difference (Fig. 4).

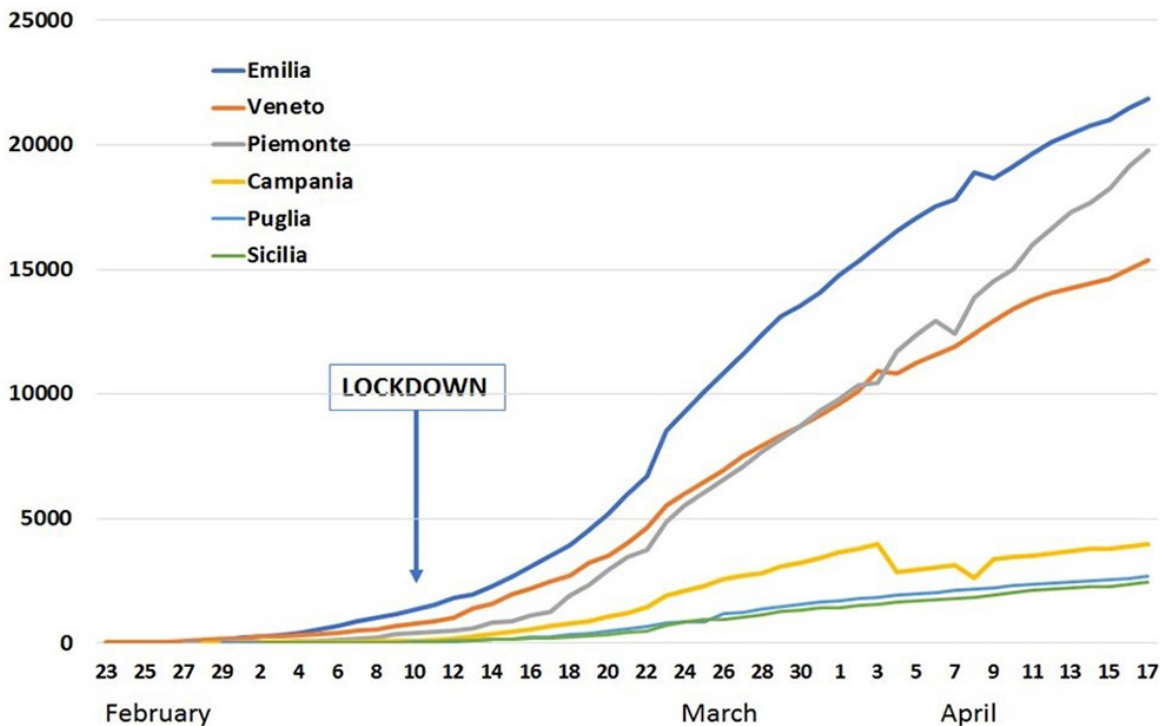


Fig. 4. The Italian "divide". The cumulative growth of COVID cases is shown in three regions of Northern Italy (Veneto, Piedmont, Emilia) and three regions of the South (Campania, Puglia, Sicily) starting from the first recorded case. The red zone was established 17-18 days after the tenth case in Northern

Italy and 6-11 days after the tenth case in the South. We decided not to include in the graph Lombardy, which, precisely because of the delays and initial errors, experienced a much more dramatic situation (resulting in about half of the deaths across the country).

These simple correlations were widely confirmed by the spread of the virus in the rest of Europe and above all in both North and South American countries. In all countries where containment strategies had been implemented late, the initial exponential increase in cases was particularly dramatic and protracted.

In Europe immediately after Italy, Spain, France and Belgium sank into the drama. In many Nordic countries, in which SARS-CoV-2 began to circulate later and countermeasures could be adopted more easily due to the specific social and behavioral characteristics of those societies, the effects of the pandemic were and still are much less dramatic.

Numbers and trends: infections and deaths

The easiest way to correctly interpret the evolution of the pandemic and to highlight the importance of effective containment measures is to start from the numbers. To simplify as much as possible we will underline only the number of deaths recorded, month by month, in the main areas affected by the pandemic.

On March 25, WHO reported a total of 4000 deaths in Asia. Most in Hubei region of China, while all the other countries recorded a few dozen deaths. It is possible to say that the countries of South East Asia immediately managed to block the chain of contagions and to contain the first pandemic wave. The epicenter of the pandemic soon moved westward to Iran where the deaths at the end of March were almost 2000, with over 100 daily deaths (1934/122). In Europe, Italy was the first country to be hit hard: within a month, approximately 70,000 cases and 6820 deaths were recorded, 743 of which in a single day (6820/743). Furthermore, the data on the number of deaths in Spain (2696/514) and in France (1100/240) began to drastically grow. In many Nordic countries the figures were less dramatic from the outset. On March 25 the deaths were 149/23 in Germany, 36/11 in Sweden, 32/8 in Denmark. Only apparently reassuring were the data in UK (422/87), Holland (276/63) and Belgium (122/34). In fact, Britain still had few cases, but it was beginning to show a worrying increase in daily deaths. In Holland and Belgium, the number of deaths was high, if compared to the small size of the population.

From such critical data, it should have been possible to predict the trend of the epidemic in the different countries, simply basing on the one hand on the modalities of increase in cases and especially in deaths (indirect index of high viral load in many involved subjects), on the other hand on the containment strategies adopted, without the need to call into question other hypothetical factors (environmental, climatic, genetic, etc.).

In this sense, the most instructive data are those inherent the American countries. Here too, at first glance, the situation did not seem worrying on March 25th: United States (673/202), Brazil (46/21), Mexico (4/0), Peru (5/3), Ecuador (27/12). But, in hindsight, the relationship between cases and deaths was rapidly changing and in the immediately following days both in the United States and in the little Ecuador there was a very rapid increase in deaths.

Nonetheless, both in the USA (and in Great Britain) and in Brazil the political leaders declared that they wanted to let the epidemic take its “natural” course: this decision was based, at least in the Anglo-American countries, on “ideological” reasons unacceptable on a moral level. Surprisingly they awoke, “darwinistically”, the sacrifice of a certain number of elderly and fragile subjects. In fact, if a pandemic virus is allowed to spread in the population, the exponential growth of cases (and deaths) risks to become rapidly catastrophic. Especially, in the face of a virus, such as SARS-CoV-2, which has the following characteristics that make it particularly insidious:

- a long period of incubation and pre-paucisymptomatic latency (7-10 days);
- the frequent a-symptomaticity of the subjects infected;
- the long duration of the infectious period.

All these factors not only facilitate the spread of the virus, but also make it difficult to assess the status quo, as the official epidemiological data is an effect of infections contracted in the previous 2-3 weeks. That's why the data were initially misleading. And that's why the initial situation was long underestimated, especially in the United States, Great Britain and Brazil. At the end of April, the number of deaths in Italy had exceeded 27,000; Spain and France had reached 24,000 (the 3 countries had about 300 deaths per day). But the data was even worse, in relation to the size of the population, in Belgium (7400/100), Netherland (4750/50), Sweden (2400/80) and especially Great Britain where within a month it had gone from a few hundred deaths to 22,000/350.

But, where the drama began to take shape in all its gravity, it was across the Atlantic: the United States passed from a few hundred deaths to over 50,000/1200 within less than a month, Brazil to 4300/200 while the data began to become dramatic even in Mexico, Peru, Chile. Worrying was the rapidity by which the data worsened: on May 3, the US had exceeded 62000/5000 deaths, Brazil 6300/428, Mexico 1972/110. While in Europe the number of infections and deaths began to slow down, with the exception of Great Britain (28.130/620) which was going to overcome Italy (28.700/470,) France (24.700/160) and Spain (25.100/270).

Table 1 summarizes the situation perfectly⁴:

Tab 1 ⁴

Countries	June 3		July 3		July 30	
	A: Total cases	B: Total/daily deaths	A: Total cases	B: Total/daily deaths	A: Total cases	B: Total/daily deaths
India	207.600	5.815/215	625.000	18.210/380	1.583.792	34.968/775
Indonesia	27.550	1.663/22	59.400	2.990/53	104.432	4.975/74
Bangladesh	52.450	710/37	153.280	1.926/38	232.194	3.035/35
China	84.600	4.650/1	85.280	4.650/0	87.680	4.665/1
Philippines	19.000	966/6	38.800	1274/74	85.486	1.962/15
Russia	432.270	5.215/178	667.880	9.860/175	834.439	13.802/129
UK	278.000	39.370/324	283.760	43.995/90	301.459	45.961/83
Italy	230.500	33.530/55	240.960	34.820/30	246.776	35.129/6
Spain	240.300	29.860/10	250.000	28.370/5	282.641	28.441/5
France	148.000	28.880/107	158.300	29.790/14	173.455	30.120/15
Belgium	58.615	9.515/19	61.730	9.765/4	67.242	9.836/0
Netherlands	46.650	5.967/5	50.360	6.110/0	53.621	6.147/2
Sweden	38.590	4.470/65	70.640	5.411/41	79.782	5.730/28
Iran	157.560	7.940/64	232.860	11.000/148	298.909	16.343/196
Iraq	7.390	235/20	53.708	2.160/110	118.300	4.603/68
Egypt	27.530	1.050/50	72.000	3.120/86	93.356	4.728/37
South Africa	35.800	755/50	168.060	2.845/95	471.123	7497/240
USA	1.800.000	107.000/760	2.671.200	127.860/725	4.323.160	148.640/1191
Brazil	526.500	30.000/623	1.448.750	60.632/1038	2.483.191	88.539/921
Mexico	93.430	10.170/237	231.770	28.510/741	402.697	44.876/854
Peru	170.040	4.630/130	288.477	9.860/183	395.005	18.612/194
Colombia	30.500	970/30	102.000	3.470/136	267.385	9.074/297
Chile	109.000	1.190/75	284.540	5.920/167	351.575	9.278/38
Ecuador	40.400	3.440/480	59.460	4.640/112	83.193	5.623/39
Canada	92.150	7.340/40	104.200	8.590/0	114.994	8.912/11
TOTAL	6.287.771	379.941/3621	10.710.105	517.877/5.032	16.812.763	662.095/5.999

Interpretations and disputes. Between negationism and conspiracy

These figures should be sufficient to understand the dynamics of contagions and pandemic expansion and to understand what happens when the dramatic potential of a pandemic virus is underestimated, and it is allowed to circulate and adapt to the new species.

Yet this has not been the case. For months the most contradictory and misleading interpretations of the ongoing pandemic have followed one another.

As already mentioned, we knew from 2015 (Menachery, V., Yount, B., Debbink, K. et al., 2015) and especially since 2017 (Hu B, Zeng L-P, Yang X-L, Ge X-Y, Zhang W, Li B, et al., 2017) that the emergence of a pandemic bat-SARS-CoV was extremely likely and imminent. Virologists and “virus hunters” had raised the alarm in many ways and “pandemic plans” had been prepared everywhere. Unfortunately, in the West, it remained dead letter. Because of the frequent and profound interpretative divergences manifested by the “experts”.

It would be difficult to try to summarize here the jumble of different and contradictory interpretations. Conspiracy theorists and negationists have dominated the airwaves for a long time: even the painful American drama did not convince them to shut up. The underlying impression is that at the origin of this dangerous muddle is a profound misunderstanding even among “experts” regarding what is a pandemic virus. Many clinicians, epidemiologists and even infectious disease specialists, in the West, have tried to interpret the evolution of the pandemic using the clinical and epidemiological data. Yet, they have not realized that a virus which has recently made the spillover –and is adapting quickly to the new host– is a form of a ticking time bomb.

In the first phase, only a small percentage of the population is severely affected, essentially in relation to the viral load (i.e. the amount of virus present in an active/proliferating form in the upper airways of infected subjects) and the conditions of their immune system. This causes serious and potentially lethal forms only in subjects who, due to predisposed conditions (Akbar AN, Gilroy DW. 2020), undergo a paradoxical immunoinflammatory reaction: Cytokine Storm, Macrophage Activation and Systemic Intravascular Coagulation (Merad, M., Martin, J.C., 2020). But, within a few months, due to minimal adaptive genomic variations of the virus, an insufficient control of the transmission chains of the infections, a changed immune reactivity in many people, the situation could change radically. In this case, as in the second phase of the Spanish flu, even slightly affected individuals to date, such as children and young people (Dong Y., Mo X., et al. 2020), could develop the systemic inflammatory reactions, which are in fact the real cause of critical cases.

This would be the so-called “worst possible scenario”, which should be taken into consideration, due to the possibility of the virus returning (as in 1918/1919) to circulate everywhere with viral loads similar to those initially registered in the most affected areas.

It is precisely in this light that the great danger linked to the many “denial” and misleading interpretations emerges. Indeed, it is also because of these controversies that political decision-makers may not act in the next months for:

1. Securing health systems, organizing alternative access strips and dedicated health departments (Miani A., Burgio E. et al, 2020);
2. Preparing adequate protective devices for all healthcare operators and diagnostic tools and therapeutic protocols finally validated and standardized (Sanders, Monogue, Jodlowski, Cutrell, 2019).

If this does not occur, the scientific community will continue to show itself unprepared to face this epochal drama in a right way.

The problem is that ideological and political approaches prevail even in these cases, as we have seen in 3 months of sterile debates and controversies. These should be set aside for the “Common Good”. There are precise biological, genetic and epigenetic reasons which determine the potential of these biological agents. Someone will say that this is reductionism, determinism: exactly what we have been fighting for decades.

Well, it is once again evident that a reductionist/molecular approach proves to be as essential as a systemic one.

The four scenarios and conclusions

As we have already said, it is difficult to make a summary of these first 6 months of the pandemic today. Even more difficult to try to imagine what will happen in the coming months or years. This is complicated because we do not yet know enough about the origins, nature, evolutionary/adaptive tendencies of this virus. We certainly learned a lot about the pathogenetic mechanisms, but not enough about the factors that determine the feared immune-inflammatory reaction, especially in young people and children, the so-called COVID-Kawasaki Disease being the most emblematic example of this (Verdoni, Mazza, et al., 2020). Even less predictable is the immune status at the population level, given that to date it would seem that even in the most affected regions protective levels of immunization would concern less than 30% of the affected population and only those that have had symptomatic forms.

Finally, if we want to try to frame the SARS-CoV-2 pandemic in a scientifically acceptable way, we would have to hypothesize at least 4 possible scenarios.

The first one is that, initially supported also by pulmonologists, infectious disease specialists, immunologists and even some virologists, of an emerging respiratory virus similar to many others, potentially not worse than a common influenza virus. Yet, it had more serious effects due to some initial evaluation errors, the late implementation of containment, and the insufficiency of intensive care units. In our opinion, a slightly more careful analysis of the epidemiological data coupled with all the biological reasons (inherent both to the virus and to the reactions of the new host), make this hypothesis absolutely unlikely.

The second scenario is the most probable or is the most accredited one to date: SARS-CoV-2 is a new bat-Coronavirus that made the spillover (as expected for years), adapting in a few months to the new host (Andersen, Rambaut et al., 2020). It is important to stress that the new virus has all the expected and feared characteristics and is capable of producing much damage. Just think of the last time a virus made the spillover and spread with similar rapidity (contagiousness) and virulence in recent history: it was 1918 and we all know the consequences.

The third scenario, now set aside for politically correct reasons, is that of a laboratory accident. Those who deal with these issues know that for years a moratorium (probably useless and even dangerous) on the experiments that generate viruses very similar to SARS-CoV-2 was claimed. Yet, similar accidents occur every year (many of which are due to human and technical errors). On a scientific level, the presence of the 8 key mutations in the sequence that encodes the Spike protein, coming from the virus of another animal, perhaps the pangolin (Tao Zhang, Qunfu Wu, Zhigang Zhang, 2020), make this third scenario plausible. For the same reasons, it is impossible to rule out a fourth scenario: that of an intentional release. Of course, this would lead us to completely unpredictable conclusions and could affect our future in an even more dramatic way (Furmanski, 2014).

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Notes

¹ *China European Respiratory Journal*, 2020; DOI: 10.1183 / 13993003.00562 -2020.

² Burgio, 2020.

³ Ibid.

⁴ Tab. 1: A: Total cases, B: Total/daily deaths. The countries currently characterized by a rapid increase in cases and deaths are highlighted (in bold). More than not the number of total cases (affected by the high percentage of asymptomatic and unrecognized cases and by the number of available/performed tampons) the most significant data are those concerning total/daily deaths. It is on the basis of these that we have selected the countries in which the pandemic is still most active.

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