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Chronicle of a Pandemic Foretold

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The emergence and spread of the COVID-19 pandemic has raised many questions and doubts, ranging from the true "origins" of the virus (SARS-CoV-2) to problems related to clinical management of the disease. Here we discuss serious concerns that have emerged about the health policy measures adopted in Italy.

In order to properly assess these issues in perspective, we provide a detailed documented chronicle of the events as they came to light.

Background

27th April 2018. During a conference organized by the Bill Gates Foundation with the prestigious New England Journal of Medicine and the Massachusetts Medical Society, Gates claimed that it was necessary to prepare for an imminent flu pandemic: "The world needs to prepare for pandemics in the same serious way it prepares for war [...]. This preparation includes staging simulations, war games and preparedness exercises so that we can better understand how diseases will spread and how to deal with responses such as quarantine and communications to minimize panic" [1]. Nothing new. Alarm about a future pandemic had already been raised long before the emergence of COVID-19, and at least since the outbreak of the SARS epidemics [2].

December 2019. On an uncertain day, the US Secret Service alerted its National Service counterpart about what was going on in Wuhan province, China. Fox News broadcast the information. In Italy the news was issued by Adn-Kronos (*Coronavirus, Fox News: 'Intelligence reports warned the Italian Government of the risks'*) [3]. The first COVID-19 patient appears to have been admitted to a Wuhan hospital on 8th December with a "mysterious disease". For seven weeks after that date, about 30,000 people per day left Wuhan for the rest of the world.

Early December 2019. Dr. Li Wenliang, an ophthalmologist in Wuhan hospital, recorded an unusual number of cases of atypical pneumonia among his patients. He posited a correlation with a virus-based epidemic associated with conjunctivitis, similar to SARS (severe acute respiratory syndrome). He mentioned this in chats with colleagues and patients. As often happens in communist regimes, he was consequently dismissed, imprisoned for a while and later reinstated. He died on 6th February after returning to his workplace to fight COVID-19. About 40 other Chinese doctors suffered the same fate: first marginalized and "silenced", then "rehabilitated" [4].

27th December 2019. Zang Jixian, a doctor in Hubei Provincial Hospital, reported to Wuhan Health Autho-

rities that a virus belonging to the SARS family was causing the infection. More than 180 patients were already infected by then, according to a South China Morning Post report [5]. This is the first reconstruction to put the Chinese authorities in difficulty [6].

The Chronicle

31st December 2019. China formally notifies the WHO (World Health Organization) of the existence of a mysterious new influenza virus.

1st January 2020. Chinese authorities confirm the first victim of coronavirus.

7th January 2020. China communicates some clinical/biological traits of the virus to the WHO and takes the first measures to contain the disease.

12th January 2020. The WHO declares that there is no scientific evidence of human-to-human transmission of the virus [7].

13th January 2020. The first coronavirus victim outside China (a woman in Thailand).

15th January 2020. The first case is identified in the USA (an American citizen from Wuhan). An analysis by the Johns Hopkins University highlights the spread of the epidemic since November 2019 [8].

16th January 2020. First public report of the Italian National Health Institute on the spread of COVID-19 recommending to "strengthen standard measures of prevention and control of infections, especially in emergency rooms and emergency medicine departments". "Between 31st December 2019 and 12th January 2020, the Chinese Health Authorities identified 41 cases of pneumonia in the city of Wuhan caused by a new coronavirus (2019-nCoV). In January 2020, Thai and Japanese Health Authorities also reported two cases of 2019-nCoV infection in people from Wuhan City. Based on the information currently available, *WHO does not recommend any restrictions on travel or commercial routes* and the ECDC [European Council of Disease Control] considers the risk of introduction of the virus into Europe to be "low"" [9].

20th January 2020. An official speech about the virus by President Xi Jinping, broadcast by many international mass media, reckons that the infection travels from human to human, as confirmed by the National Health Commission of Beijing. On 20th January, Chinese scientists describe the genomic structure of the virus in detail (the virus was isolated on 7th January and the sequence was made public on 9th January 2020) and its similarities to SARS, as reported in an article published by *Nature* [10].

Significantly, the first officially ascertained case dates back to 1st January, and five more patients have been studied. Considering the amount of work this involves (the responses of numerous animal species to the virus were also highlighted in the study), we wonder how this research could have been conducted, completed, written and sent in less than 19 days. Such work generally takes much longer (the data must also be verified and replicated) and it is truly amazing that no one pointed out this discrepancy: how could the Chinese laboratories – even considering the understandable "urgency" and political pressure – have produced that result in less than three weeks? Actually, the entire sequence of events is highly suspect. The first official case is identified on 12th December 2019; the next day the Wuhan Animal Market is closed; 6 days later the virus has been isolated (!) and after two more days its sequence is published [11], after testing the virus on a battery of cells from different animals (including humans), and identifying the receptors to which the virus binds! Moreover, on 16th January, swabs and kits for RT-PCR analysis are distributed throughout the state of Hubei. Between 19th and 21st January, all Chinese provinces and regions are supplied with them. It is even more surprising that these kits were already supplied in advance to the WHO as of 12th January. Many of these procedures are compatible with the times reported, but not all of them. The suspicion is that the virus *was known and had already been studied before 9th January, when China officially sent data on the virus to the WHO*, as described in the joint WHO-China report (24th February) [12].

These questions fuel doubts about the Wuhan laboratory and raise new questions about the reliability of Chinese sources and reports. In particular:

1) *Contamination*. The Wuhan laboratory has been the subject of several surveys, as it was suspected to be responsible for accidental contamination. An article from Nature in 2017 details these risks [13]. The laboratory was planned in 2003, and built in 2004 with the direct participation/support of France (which boasts some of the best skills in the world in this sector). France also trained several young Chinese scientists in a laboratory in Lyon. In recent years, there have been accidental di-

spersals of SARS viruses from Beijing biosafety level 4 laboratory (China has two BSL-4s). China is currently planning two more BSL-4s with the pretext of studying SARS, claiming to have a large number of monkeys to test on. However, as international observers note, "We are not convinced of the need for more than one BSL-4 in mainland China". Ebright suspects that the expansion is a reaction to the networks in the United States and Europe, which he says are also unwarranted. "These facilities are inherently dual use", he says. The prospect of ramping up opportunities to inject monkeys with pathogens also worries, rather than excites, him: "They can run, they can scratch, and they can bite" [14]. The real boulder is in fact the lack of identification of the intermediate link of the virus, the one via which the virus passed from bat to man, "jumping" species (spillover). This is what renders plausible the hypothesis that the virus escaped from the Wuhan laboratory to infect humans directly. This is a critical question. If there is no evidence to explain the (hypothetical) spillover, other explanations remain in place, including accidental release of the virus from the Wuhan laboratory. Indeed, zoonotic spillover should not be given undue credit, because the epidemic curve is consistent with substantial human-to-human transmission [15]. Obviously, this possibility raises a number of embarrassing concerns.

2) *Viral manipulation: was COVID-19 "manufactured"?* This question arose because it is not clear how the virus, normally hosted by bats, could pass to humans without first adapting to an intermediate host. The question has not yet been answered. A study (hastily) published in *Nature Medicine*, excluded any intentional manipulation but left many hypotheses open: "Although the evidence shows that SARS-CoV-2 is not a purposefully manipulated virus, it is currently impossible to prove or disprove the other theories of its origin described here" [16]. It is however indisputable that COVID-19 comes from SARS (which was studied in Wuhan); indeed, the official name incorporates this derivation. It is also strange that "the overall molecular structure of this virus is distinct from that of known coronaviruses but most closely resembles viruses found in bats and pangolins that have been little studied and never known to cause humans any harm" [17]. Furthermore, Chinese scholars write: "According to researchers from Nanki University in Tianjin China, COVID-19 contains a strange HIV-like mutation that may make it more contagious and give it properties not found in other coronaviruses. The Chinese study builds on earlier research in India that concluded that the disease was unlikely to have originated in nature. This comes amid speculation that COVID-19 originated in a Chinese research lab located in Wuhan. While these theories remain unconfirmed, they should not be dismissed as conspiracies" [18]. Indeed, previous Hantavirus outbreaks have been associated with laboratory rats in Yunnan (China) [19], while genetic modifications have purportedly been performed on different strains of coronavirus. Namely, the receptor-binding capacity of coronaviruses has been investigated by combining a human immunodeficiency virus-based pseudovirus system with cell lines expressing the ACE2 molecules of humans and animals [20], thus enabling the coronavirus to enter human cells while native viral proteins are unable to do so. Indeed, it is quite unlikely that a virus acquire such unique insertions naturally in a short time. This structural change may also have increased the range of host cells that 2019-nCoV can infect. A hypothesis of this type was recently supported by Nobel laureate Luc Montagnier and bio-mathematician Jean-Claude Perez, who suggested that the new COVID-19 could be the fruit of inexperience in an attempt to produce an anti-HIV antibody [21]. Several scientists have rejected this statement with outrage; however, since the claim comes from the very scientist who discovered and isolated the HIV virus, the hypothesis deserves to be held in high regard.

3) *Distorted chronology*. The temporal reconstruction of the events is manifestly distorted, as stated by Dr Li Wenliang, who already in a chat of 31st December 2019 spoke of "six patients with identified viruses belonging to a SARS-like subtype, of the coronavirus type" [22], suffering from conjunctivitis and atypical pneumonia. This admission documents how a pre-characterization of the virus had already been done before 20th January. Dr Li recommended that friends and relatives take precautions. Two days later he was interrogated by the police, warned by the authorities not to spread alarm and removed from the hospital, only to return a few days later. A similar fate has befallen other doctors. In fact, according to investigations by the Johns Hopkins University, recently confirmed by the South China Morning Post [23], the first cases of SARS-CoV-2 date back to early November 2019 (3rd-17th November).

21st January 2020. China decides to isolate the Wuhan Region with blockade of trains and planes.

22nd January 2020. The victims of COVID-19 in China are officially 17. Meeting of the operational Task Force of the Chinese Ministry of Health.

23rd January 2020. Two Chinese tourists disembark at Malpensa Airport in Milan. They arrive in Rome on 29th January, where they are stopped and identified as infected with COVID-19. The WHO, for its part, organizes a meeting to decree an emergency, however, China blocks that step. WHO General Director, Tedros Adhanom Ghebreyesus, who was accused of "hiding" three cholera epidemics when he was Minister of Health in Ethiopia [24], flies to Beijing to discuss the matter with the Chinese President. On his return, he praises China for its efforts in health management and declares that there is no reason to "interfere" with the free movement of persons and goods by freezing transport to and from China.

24th January 2020. It is revealed that the first COVID-19 patient in China was hospitalized in Wuhan on 8th December 2019, recorded as having a "mysterious disease". From that moment on, for seven weeks, about 30,000 persons per day left Wuhan for the rest of the world. A suspected case of COVID-19, a musician who had returned from Wuhan, is identified in Parma in January [25]. In the same days, the first three infected persons are discovered in France, one coming from Wuhan [26]. The escalation of cases is worrying. In the face of these signals, the Western media shows skepticism and tends to minimize the "accidents". Italian newspapers prefer to "constrain" any form of "alarmism". According to Il Foglio, "Concern and caution are one thing, but the alarmism that has been raging in the last few days is proliferating faster than the virus and risks doing serious damage. The concern is also about China: the regime tries to appear responsible but according to various experts the precautions it has taken so far have been too weak and too late" [27]. Faced with this news, it is disarming to read in the *Giornale della Protezione Civile* on 24th January: "Italy has a plan against the coronavirus, but so far no alarm" [28].

25th January. China declares a 60% increase in infections in two days [29]. The Americans evacuate from China [30].

27th January. Israeli analysts link the coronavirus emergency to the Wuhan laboratory, suggesting that an "engineered" virus could have escaped, by mistake or through incompetence, and infected the town's animal market [31].

28th January. A case of COVID-19 infection is identified in Germany in a person who has never been to China [32].

30th January. The WHO declares COVID-19 a "Global Health Emergency" [33]. The first two cases are identified in Italy.

31st January. The Italian Council of Ministers decrees a state of emergency for six months. The Emilia Romagna Region organizes a "task force" and decides to set up two "rooms for restrictive isolation per Province, reserved for serious and stable patients", one with respiratory support. It also decides "not to isolate symptomatic patients from Southeast Asia, except those from the Wuhan area" [34].

2nd February. The Chinese community of Bologna has been procuring medical supplies to send to Wuhan for two weeks (10 thousand masks, 550 coveralls and 10 thousand pairs of gloves) [35].

15th February. A Chinese returning from Wuhan with COVID-19 dies in France [36].

22nd February. The Italian Council of Ministers launches the first real decree to counter the transmission of the coronavirus.

16-24th February. Although the WHO has declared a "global health emergency" as of 30th January, only now (16th February) does a WHO delegation travel to China, where it remains for nine days to conduct an extensive investigation [37]. Its report highlights that sporadic cases of abnormal pneumonia, suspected to be caused by a SARS-like virus, had been reported since October 2019. The second critical point concerns the origin. Since the natural reservoir of the virus is bats, the intermediate host through which the virus reached humans has not been identified. Failure to find the missing link leaves open the possibility that the virus escaped (accidentally) from the Wuhan BSL-4 laboratory. The report also highlights that health workers are particularly exposed to the infection (2055 health care workers are reported to be infected in 476 hospitals in China) and require special and urgent precautions. Indeed, on 20th February, China implements additional measures to protect physicians. The WHO report is in the hands of the Italian government as early as 25th February, yet no measures are taken to protect health professionals. Overall, however, the WHO report is contradictory:

a) Traditional belief in the benefits and miraculous virtues of certain foods of animal origin has nourished unhealthy and dangerous dietary habits among Chinese

citizens, such as "jinbu" or intake of meat from live animals or otherwise without prior sanitation. Numerous reports indicate that the experimental animals used in Wuhan's BSL-4 laboratory are often "resold" to the local market for extra earnings, instead of being properly disposed of by cremation, as the law requires. One Beijing researcher, now in jail, made the equivalent of a million dollars selling monkeys and rats on the live animal market, "whence they likely wound up in someone's stomach" [38]. The report does not suggest any recommendation regarding this critical question.

b) The report lavishes embarrassing flattery on the Chinese regime for the effectiveness and promptness of measures that nipped the epidemic in the bud, making it unnecessary to issue a general alarm. On the other hand, however, the report cannot fail to detect that the virus is "highly contagious, can spread quickly, and must be considered capable of causing enormous health, economic and societal impacts in any setting". The report does not stigmatize the fact that the Chinese authorities deliberately decided not to count asymptomatic patients among the infected: this underestimation has enormous consequences in terms of epidemiological evaluation. In fact, as early as February, data silenced by the Chinese government clearly indicated that more than a third of positive patients are asymptomatic and vehicles of infection [39]. Keeping this information secret objectively favored worldwide spread of the virus and weakened any strategies for containing the epidemic, since by definition and at the indication of the WHO, asymptomatic cases were not traced or tested. This indication was followed by the *Italian Consiglio Superiore della Sanità* on 26th February [40]. According to an analysis reported by Science [41], asymptomatic cases caused 79% of clinically detectable cases. The report finally borders on paradox when it considers other countries unable to take the measures adopted by China with equal efficacy and determination: "Much of the global community is not yet ready, in mindset and materially, to implement the measures that have been employed to contain COVID-19 in China. These are the only measures that are currently proven to interrupt or minimize transmission chains in humans". Finally, the report asks other countries to activate the "Emergency plan", immediately at maximum level: "Prepare to immediately activate the highest level of emergency response mechanisms to trigger the all-of-government and all-of society approach that is essential for early containment of a COVID-19 outbreak".

In the same period in Italy, government officials tried to minimize the infection. Towards the end of February 2020 certain politicians declared that there was no cause for concern, since the disease in question was "little more than a flu". The Mayor of Florence Maurizio Nardella organized a dinner with many guests in a Chinese restaurant to dispel "legends" about the risk of spreading the disease. Slogans in the month of February were "Embrace a Chinese" and "Reopen Milan" (27th February, "Coronavirus, Sala calls Conte: "Let's reopen Milan as soon as possible") [42]. Heedless of the serious danger posed by the unfortunate situation already existing in Italy, those who called for urgent measures to contain the contagion were dubbed "fascists" or "racists" by exponents and fans of the current parliamentary majority.

23rd February, 2020. The Italian Government issues the first containment measures, without giving any details [43].

11th March 2020. The WHO declares the status of pandemic, when coronavirus cases have reached 287,000 worldwide, on five continents [44].

Data uncertainties: diagnostic unreliability and the limits of statistical models

From the outset, the management of the ongoing epidemic has been characterized by four orders of uncertainty pertaining to the reliability of the data. This is of no secondary importance, because the narrative of the mass media, government decisions and opposition responses were based on data, which was on the whole absolutely unreliable. Doubts regarding the available information include:

1) *Data from China*. We know today that the first cases of COVID-19 were recorded in early November 2019. The Chinese authorities began to study and isolate the virus long before 9th January 2020, when they sent their preliminary report to the WHO. Uncertainty also remains regarding the true death rate and the incidence of COVID-19 [45].

2) *Italian data*. In the absence of a population-sample-based screening program (which can then be extrapolated to the general population) or a systematic

investigation in the most affected region (Lombardy), assessment of the spread of the epidemic (number of people infected regardless of their clinical status) was absolutely inadequate. This not only led to underestimation of the extent of the infection, but also to gross calculation errors, especially regarding the lethality of COVID-19. Lethality is obtained by calculating the ratio of the number of casualties to the number of positive cases. If the denominator increases, the value of lethality decreases. Current estimates suggest that the number of infected people greatly exceeds the number of positive tests, e.g. by a factor of 35 [46]. Moreover, there is growing evidence that the death figures reported daily by Italian officials may be grossly underestimated [47].

3) *Technical limits*. Technical limits concern how the data was collected, the inclusion criteria (especially with regard to cases of death) and the reliability of the analytical determinations (buffers, virus genomics etc.). To limit the example to China, out of 76,314 cases reported in an extensive review, 22.4% were classified as "suspect cases", 14.6% as "clinically diagnosed" and 1.2% as "asymptomatic" [48]. This means that 37% of the cases reported in Chinese statistics so far were only diagnosed on a clinical basis ("suspect cases" according to the WHO definition). Yet mainstream information to the world population presented them all as "firmly established". Antibody testing, which should have been considered fundamental for confirming or refuting acute infection, was ignored until the end of April. This technique was available from the beginning, but was not used until much later. Confirmation of cases was mainly based on nasopharyngeal swabs and gene amplification by RT-PCR, a non-validated, non-standardized technique that seems to give many false positives and false negatives [49]. Another concern about PCR-based tests is that there has not been enough time to assess their sensitivity and specificity. Based on personal communications with colleagues, a significant proportion of patients who meet clinical and chest CT diagnostic criteria for COVID-19, including many hospitalized patients, tested negative for viral RNA [50]. Other common respiratory etiologies, such as influenza, were excluded but remain "suspect" cases that may be false negative to PCR [51]. In some patients, the virus may be present in lower respiratory secretions but absent in the upper respiratory tract. With current tests, it is therefore difficult to obtain a meaningful assessment of the percentage of symptomatic infected patients [52, 53]. There is also a huge problem relating to the attribution of causes of death. First, only a few autopsies have been performed, and this makes it impossible to correctly ascribe the cause of death to the virus and to understand the pathogenic mechanisms involved. Secondly, because the lethality risk data is artificially overestimated when pre-existing pathologies – often more serious than the COVID-19 infection – are discarded. In Italy, the "all in" criterion was used, whereas elsewhere, as in Germany, the more rational approach of assessing the predominant "causative" role of the virus was applied. This discrepancy could explain the hugely different lethality rate between Italy and Germany at the end of March 2020 (11.40% versus 0.9%). Then if we want to evaluate mortality (as distinct from lethality), we have to compare all deaths recorded in a certain region with those recorded in previous years to verify whether the epidemic caused (and to what extent) more deaths than expected.

4) *Ambiguous and confused communication*. Finally, these elements influenced the communication model adopted by the government, generally characterized by an absence of officialdom (interviews in the context of entertainment programs, TV lounges and talk-shows), based on contradictory announcements (statements not followed by concrete acts or worse still denied shorty after), improvised (communications of closures and lockdowns not associated with the necessary containment measures) and based on alarmism rather than on the need to inform and equip the public. Thus, the habit of communicating the "war bulletin" every day at a given hour, together with the uninterrupted procession of experts, each eager to give his own version, aroused concern far beyond what was necessary and desirable, as well as anxiety and confusion.

Failure to act and political inadequacy

a) *The World Health Organization* (WHO). The behavior of the WHO appears to have been based on a serene temporal reconstruction, discreditable to say the least and showing no hint of self-criticism or self-reproach. The WHO has shown culpable omissions, delays and inadequacies:

1) The WHO did not monitor the Wuhan laboratory, despite the fact that its activities had long been targeted by the scientific community.

2) It did not promptly call a state of alert, necessary on isolation of the new viral strain (9th January 2020).

3) It issued the pandemic alert about 40 days late (15th January), when besides the Wuhan outbreak, full-blown cases of COVID-19 were already known in Thailand, Japan and the United States. By 20th January, it was clear that the infection was transmitted between humans via the respiratory route. Yet in its press releases and the final report downstream of the control visit to China (24th February), the WHO persisted in declaring the situation to be under control and in praising China for the measures implemented. At the same time, the WHO firmly stated that blocking flights to and from China "was an error" [54]. This position was even reinforced by the Director-General, Tedros Adhanom Ghebreyesus, according to whom "these limitations risk increasing fear and discrimination and have poor public health results" [55].

4) In the meantime, the WHO was ignoring alarms from Japan, Korea and Taiwan. All too ready with praise for China, incredibly the WHO did not indicate the efficient protocols implemented by Korea and Taiwan as a model to stem the epidemic. Even more incredible, it deliberately ignored the alarm launched by Taiwan in early December about the possible outbreak of an epidemic from China [56].

In summary, there is no doubt that relations between China and the WHO are not transparent. As already happened in 2003 for SARS, China has clear responsibilities regarding emergence of the epidemic, its worldwide spread and other countries' delay in dealing with it.

b) *The Italian Government*

The Italian government continues to show hesitations and inadequacies that must be clearly denounced.

First of all, it shows a general lack of awareness of the epoch-making problem of dangerous epidemics. At the centenary of what is known as the Spanish flu (1918-1920), re-examined in several recent books and reports, its absence of understanding of the danger of periodic flu-based epidemics is incomprehensible [2, 57, 58]. The Lancet has appropriately stigmatized this incompetence on the part of political authorities by speaking openly of "trained incapacity" [59]. The Italian government is no exception: like other States it demonstrated that it had failed to learn from previous experience and failed to heed the recommendations of the scientific community, which has been expecting a new flu pandemic since the turn of the century [60]. It is embarrassing, to say the least, that the Italian government was late in activating the National Plan of Preparedness and Response to a Flu Epidemic (updated in 2016) [61], despite widespread alarm. The objective of the Plan, articulated in six activation phases, is to prepare the country to deal with an epidemic/pandemic threat. The plan was conceived as a resource that could be brought into action, even in the absence of alarm issued by the WHO. The plan remained inactive, despite outbreaks of atypical viral pneumonia in many areas of Lombardy, Veneto and Emilia Romagna in December 2019 [62]. Furthermore, as early as 28th December, 40 abnormal cases of viral pneumonia were reported in Piacenza hospital [63]. A subsequent study by the University of Milan pinpointed onset of the epidemic in Italy between October and November, well before the first confirmed case at Codogno [64]. These reports prompted the Ministry of Health to issue a specific decree on 5th January, warning about the possibility of an unusual "flu epidemic", and requesting special attention to viral pneumonia coming from China [65]. The alert, reiterated on 12th January, continued to link virus and epidemic, but paradoxically highlighted that based on information received from China, the WHO was "reassured by the quality of the ongoing investigations [in China] and response measures implemented in Wuhan." Finally, on 16th January, we witness a turnaround, a real manipulation of the truth, in a document that goes back to talking about a possible epidemic but the link with China is deleted and replaced with "Japan", the source of the epidemic ("Japan (ex-China)") [66]! To sum up, the Plan for the management of pandemics was ignored, then activated late and incompletely, as pointed out by the Italian press [67].

Concluding (preliminary) remarks

In September 2019, the Johns Hopkins Center for Health Security issued a long document on the dangers of a forthcoming flu pandemic, made increasingly probable by globalization phenomena and unsafe handling of animals and the meat market, which significantly increase the risk of transmission of zoonotic disease to humans [68]. We had a "taste" of these dangers with the epidemic of bovine spongiform encephalopathy (BSE, also known as mad cow disease) in 2001, and later with

the SARS, MERS and other avian epidemics since 2003. The current epidemic is not exactly an "unexpected" event that took the authorities by surprise. Scientists and technicians of the state administration knew perfectly well that it could happen, and in a sense, they considered it an imminent possibility. On 11th March 2019, *La Repubblica*, a major Italian newspaper, wrote: "It is not a question of whether but of when (the pandemic) will arrive. The Global Influenza Strategy is the newly launched program to address risk. It has two objectives: investing in research and improving surveillance and intervention systems" [69].

The COVID epidemic has highlighted two other fundamental limits of healthcare organization in Italy:

1. *Inadequate support to scientific research*. For years, Italian scientific research has received inadequate funding compared to other countries in the European Union, despite its high level and productivity (three times that of Germany on a quarter of the funding). Four months after the outbreak of COVID-19 and even now, few resources (less than 20 million euro) have been allocated for the scientific emergency related to COVID-19.

2. *Shortfalls in Italian healthcare architecture*. In recent years the concept of medicine inherited from the great Greco-Roman and Christian tradition has been demeaned. Hospitals, once known as *Hôtels de Dieu*, have become Business Companies for Health (*Azienda Sanitaria*), where decisions are made and evaluated on the basis of financial and management efficiency criteria. This destroyed territorial (precinct) medicine, and created multi-specialist centers of attraction, conceived as all-inclusive healthcare terminals for entire macro-regions. Territorial medical units enable better care and management of patients in the home setting. They also make technical and financial resources available for diversifying health services and their quality. In particular, the need for more intensive care units had been known since 2012, when the Monti government cut about 2/3 of the beds. Sadly, nothing was done to remedy this shortage and even in the first days of March nothing happened immediately. Another aspect is the gradual disappearance, since the 90s, of the term "prevention" from health managers' vocabulary. The concept of prevention flourished in the 70s and 80s to address complex issues such as pathologies caused by environmental pollution, occupational exposure, as well as degenerative (cancer) and metabolic (obesity, diabetes) diseases. Sacrificing the paradigm of prevention meant underestimating the risks of foreseeable new pandemics.

However, the COVID-19 outbreak offers an opportunity to rethink the health model of recent decades, including the role played (or that should have been played) by certain international organizations.

1. *The European Union*. The EU made disparate belated decisions, and indeed shone for the lack of coherent measures. No meeting was organized to specifically address the SARS-CoV-2 emergency, and the European Commission's constituent program was largely overlooked, particularly in its capacity to cope with "emerging global threats" [70].

2. *Finally the WHO*. The WHO is guilty of remaining silent and underestimating the danger, as well as covering China's errors and delays. China's behavior has been ambiguous: we still do not know with certainty when the epidemic broke out, how many deaths it caused and where the virus originated. Certainly Chinese research in the field of transgenesis and molecular biology has long been the subject of attention due to its ethical and safety implications. Over the years, Chinese researchers have too easily circumvented safety rules and ethical principles, in many cases incurring criticism and criminal convictions, as in the case of Dr He [71]. The risks associated with the possibility of pandemics related to inappropriate gene manipulation of viral and bacterial strains have been the subject of many studies [72]. For too long, "preparedness strategies for public-health emergencies have been neglected, and communities remain ill equipped to face a sudden epidemic, let alone a global pandemic. Perhaps the looming specter of a potentially devastating pandemic will kill off this false sense of security, and concentrate the minds and budgets of both governments and research communities towards preventing another superbug scourge" [73].

The real possibility that this scenario could materialize calls for application of the precautionary principle, in the spirit of the Cartagena Convention (1992). It is still not too late to propose a moratorium on projects of transgenesis and genetic modification of viruses and potentially pathogenic bacteria.

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