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General Critical Points of Emergency Response and Management: Experience with Biological Agent of the Class A in Italy, Lombardy

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ABSTRACT

Background: *Since 2019 many reviews, opinions or letters to the editor concerning the Covid-19 pandemic and biological threat have been published. The fast passage from the delimited to the global extension of the threat, observed during the Covid-19 pandemic, lead to the overturn of the health care systems and then of the concept of biological threat management. The Covid-19 experience shows that the continuous burst-outs worldwide in different time, the biological characteristics of SARS-CoV-2, the peculiarities of every single national or regional context and global extension allow to apply basic rules only partially and require a complex and flexible multidisciplinary approach. Lacking historical data and comparability with other events of this type, different contexts and health care systems, associated to the complexity of the phenomenon, makes this issue difficult to approach in a standardized way.*

Materials and Methods: *We describe standard basic definitions and protocols concerning biological threat, emergency, emergency protocol and Global Catastrophic Biological Risks and report an overview of general critical points of emergency response and management, based on known principles and our experience with SARS-CoV-2 as a biological agent class A in Lombardy in 2020.*

Conclusion: *The complex threat as Covid-19 pandemic requires an open-minded multilevel approach, based on attributes as primacy of life, risk based or shared responsibility. The standard approach to a biological threat became one of the numerous possible scenarios. There are critical passages in every emergency system related to the specific social, economic, political, biological – medical context, as determined by a complex emergency. The population at risk of transmission and the population not affected by the emerging pathogen resulted as important as the ill part of the population, determining indirectly shifts in emergency management. The risk-benefit ratio and the availability of the resources becomes the first criteria, while absolute numbers became a historical issue.*

Keywords: *emergency, emergency protocol, CBRNE, emergency management, Global Catastrophic Biological Risk, biological agent of class A, SARS-CoV-2, strategic gap, COVID-19*

INTRODUCTION

Since 2019 many reviews, opinions, articles or letters to the editor concerning the Covid-19 pandemic, biological threat and the approach to the biological threat have come out [1]. The approach to the biological emergency is defined by protocols of CBRNE type.

Two major groups of biological threats have been cited and treated since 2020: emergencies and global catastrophic biological risks (GCRs).

Some authors treated the evolution of the GCBR, emerging and converging GCBR [2], failures with Covid-19 on the international level [3] or past, future or potential future

biological threats [4][5]. The perspectives of facing Covid-19 in the first European hot zone (Lombardy), dated 2020, were partially described [6].

New technologies in the field of GCBR have been presented. The term HCIDs, high consequence infectious diseases [7] or PHEIC without and PHEIC with GCBR potential [3] appeared. Concepts to cover the gaps in specific categories were published, for example in biorisk management [8].

The fast passage from the delimited to the global extension of the threat, observed during the Covid-19 pandemic, lead to the overturn of the health care systems and then of the concept of biological threat. Covid-19 experience shows that the continuous burst-outs worldwide in different time, the biological characteristics of SARS-CoV-2, the peculiarities of every single national or regional context and global extension allow to apply basic rules only partially and require a complex and flexible multidisciplinary approach.

Materials and Methods

We describe standard basic definitions and protocols concerning biological threat, emergency, emergency protocol and Global Catastrophic Biological Risks and report an overview of general critical points of emergency response and management, based on known principles, and our experience with SARS-CoV-2 as a biological agent class A in Lombardy in 2020.

Emergency, Emergency Management, Emergency Protocol

We define an emergency an event, actual or imminent, which endangers or threatens to endanger life, property or environment, and which requires a significant and coordinated response. "An emergency with serious disruption of the functioning of a community or a society at any scale due to hazardous events interacting with conditions of exposure, vulnerability and capacity, leading to one or more of the following: human, material, economic and environmental losses and impacts" is denominated a disaster. Catastrophic disaster means an event that overwhelmed the technical, non-technical, social systems and resources and has degraded or disabled governance structures, strategic and operational decision-making functions. Emergency response system and management are based on attributes as primacy of life, comprehension, collaboration, coordination, flexibility, risk based, shared responsibility, resilience, communication, impartiality, or constant improvement, which make new approaches possible [5].

The following very short summary mentions the most significative general basic issues and terms of any national emergency (Chemical Biological Radiological Nuclear Explosives) protocol:

1. Activation of the emergency network, usually activated by first responders; the detection of outbreaks and their; appropriate infection control practices to assess the adequate management of post exposure patients; laboratory support and confirmation; patients, visitors, and public information; agent-specific recommend-dations within the limits of privacy and human rights;

2. Institution-specific response plans should be prepared in partnership with local and state health departments. Health care facilities should determine their readiness needs, which may range from notification of local emergency networks and transfer of affected patients to the proper acute care facilities, to activation of comprehensive communication and management networks. Hospitals may have the first opportunity to recognize and initiate a response to a biological threat related outbreak [9].

3. Public health preparedness is based on outbreak response and prophylaxis plan: prevention of the spread; drugs; vaccines and nonpharmaceutical intervention to reduce transmission; illness and deaths, and clinical care [10].

On the European level health care governance within the European Union is predominantly a competence of the individual member states and this issue is provided through Article 168 of the Treaty on the Functioning of the European Union (TFEU). Alerts arrive through the Early Warning and Response System (EWRS).

Globally the coordinator role actually belongs to the WHO. The WHO emits recommend-ations and guidelines about Public Health Emergency, based on stated traditional epidemiological and bio surveillance principles and International Health

Regulations dating back to 1969 and several other rules [11]. The global management of biological and/or bioterrorist threat became critical during Covid-19 pandemic. The policy of the States to spread and share data on the detailed epidemiologic situation has been discussed.

Noteworthy, the emergency management starts when the ordinary management fails, not only for the disproportion of the number of victims/patients and the resources, but for the late recognition of the risk and the incorrect risk assessment in every single context. Then the functional distress of the society affected by a threat may become one the criteria.

Global Catastrophic Biological Risks and New Technologies Addressed to GCBR

Global diffusion of SARS-CoV-2 suggested a global catastrophic biological risk (GCBR). Cameron expressed her doubts, lacking preparation to the GBCRs and strategy gaps in 2017 [2]. The failures in Covid-19 international management were discussed, for example a non-alarmist approach and lacking sensitivity of WHO to the threat [3].

Lately new approaches to cope the GCBR's appeared. GCBRs represent a subset of global catastrophic risks (GCRs). GCRs can come by the natural world but more commonly they are thought as coming from abuses or misuses of man-made technologies. Frequently cited examples of GCRs include nuclear war, climate change, and pandemics of naturally occurring or deliberately engineered pathogens [12] [13] [14] [15].

The Global Risks Report 2021, 16th Edition (World Economic Forum) defines the global risk as an uncertain event or condition that, as it occurs, can cause significant negative impact for several countries or industries within at least the next 10 years [16].

As Schoch-Spana reported, The Johns Hopkins Center for Health Security's working definition of global catastrophic biological risks (GCBRs) is: "those events in which biological agents - whether naturally emerging or reemerging, deliberately created and released, or laboratory engineered and escaped - could lead to sudden, extraordinary, widespread disaster beyond the collective capability of national and international governments and the private sector to control. If unchecked, GCBRs would lead to great suffering, loss of life, and sustained damage to national governments, international relationships, economies, societal stability, or global security". The events that don't necessarily carry the potential to cause millions of fatalities, may be considered GCBRs. This would be a distinction from prior definitions of GCRs that do have absolute fatality numbers as part of the criteria" [12].

Global Risks Perception Survey 2020 published in The Global Risk Report 2021, reports infectious diseases in first position as a clear and present danger or short-term risk (0-2 years), followed by livelihood crises (both societal risks), and extreme weather events (environmental risks). Terrorist attack (geopolitical risks) in 7th position. The top risk by impact were perceived infectious diseases, followed by climate failure and weapons of mass destruction [16].

According to the Global risks perceptions 2022 have been perceived societal risks – "social cohesion erosion," "livelihood crises" and "mental health deterioration" as those that have worsened the most since the Covid-19 pandemic began. The most severe risks on a global scale over the next 10 years were identified climate action failure in the first place, the infectious diseases in the sixth position [17].

Following examples of past biological threats may fulfill the characteristics of GCBR or potential GCBR, at those times: H1N1 pandemic in 2009 in Mexico [18], H5N1 epi-zoonotic 2005 – 2007, HIV and AIDS [19], Influenza pandemic 1918 – 1919 [20], Bubonic Plague in the 14th century [21], The Anthrax Attack, New York, 2001 [22], Smallpox Epidemic on the western hemisphere in 1492. The smallpox epidemic in 1492 reduced the human population by 90% over a century. The primary infection in pediatric population had a mortality rate of 30%. The vaccination started in 1972, the eradication of smallpox was declared in 1977. Today the smallpox vaccination is not routine, the disease could be a potential GCBR [23].

Boyd and Wilson contend that the important distinction is not between lesser or greater PHEICs but between PHEIC without and PHEIC with GCBR potential [3]. Both last two terms by-pass the definition of biological threat, but imply the correct emergency management.

The main technologies addressed to GCBR should slow the transformation of a biological threat in GCBR. They concern recognition and characterization of an emerging biological event to prevent the spread, drugs, vaccines and nonpharmaceutical intervention to reduce transmission, illness and deaths, and clinical care, especially if we talk about pathogen with airborne transmission as SARS-CoV-2. 15 technologies were highlighted in 2018, for example Microarray patches for vaccine administration, self-spreading vaccines, ingestible bacteria for vaccination, self-amplifying mRNA vaccines, drone delivery, Microfluidic devices, handheld mass spectrometry, cell-free diagnostics, etc… [4]. They principally cover, technologically improve and accelerate the emergency management, biosurveillance, production of standard mitigation countermeasures (MCMs), may be applied during all the phases of an epidemic/pandemic, in base of the alert grade. Their use may not be reserved only to infected patients. They may serve as a precious instrument to manage and treat the people not affected by emerging pathogen, for example the fragile and high-risk patients or patients with chronic pathologies, if a droplet, airborne and oral-fecal transmission is considered, or a reasonable resource management required.

SARS-CoV-2 And COVID-19 Briefly

One of the first estimate crude numbers of clinical case fatality rate published by WHO in April 2020, was over 3%, which increased with age and rising up to 15% roughly or in patients over 80 years [24]. Johns Hopkins University of Medicine reported in April 25, 2021 2,2% [25], Coronavirus disease 2019 case surveillance, United States, published 5% for the period January 22–May 30, 2020. The distribution of the cases and deaths is not ubiquitous worldwide [26].

The origin of the virus is still unclear, both natural and artificial genetic changes were not excluded [27]. Some studies have reported the bats as natural reservoirs for potentially pathogenic SARS-like CoVs [28] [29] [30] [31], whereas other document that the so-called fur in cleavage site in the spike protein of SARS-CoV-2 confers to the virus the ability to cross species and tissue barriers, but was not previously observed in other SARS-like CoVs [27][32]. However, some authors and national and international institutions work with the hypothesis of a naturally occurring disease with unprecedented global impact [7].

Table1. *Characteristics of SARS-CoV-2 as biological agent, comprehensive view, as known in 2021*

Type Biologic agent class	**Virus**
Biologic agent class	A
Global mortality rate	2%
Basic reproductive number R0	2 – 4
Case Fatality Rate (CFR)	1 -15% uncorrected
Infection Fatality Rate (IFR)	0,3-1,3 %
Recovery	mild cases 2 weeks, severe cases 6 weeks
Long-term sequele of the disease	Yes
Social disruption	Yes
Special health preparedness	Yes
Economic impact	Yes
Pathogenic potential	Evolutive
Risk Group	RG-3
Biosafety Level	BSL-3 [33].
Animal Housing Biosafety Level	ABSL-3 [34].
Host Range	humans, ferrets, cats, dogs, mink, and primates
Routes of Exposure to Humans	close contact, person-to-person spread, respiratory droplets, airborne transmission
Infectious Dose	Unknown
Vaccine	Yes
Specific prophylaxis	None available

SARS-CoV-2 is a high priority biological agent of class A according to the criteria of US CDC [35]. As of 9 November, 2022, 6.583.588 deaths and 630.601.291 confirmed cases were registered [36]. Long-term consequences include the post-acute Covid-19 syndrome, Covid Stress Syndrome or severe thromboembolic, cardiovascular and neurologic complications of the disease [37] [38] [39] [40] [41].

Critical Points of Emergency Management and Response, Emerged During and After Covid-19 Pandemic

The emergency response to the biological threat of any type is based on the extension of the event – we may treat cases, clusters of disease, epidemics or pandemics according to the biological/bioterrorist class of the agent in the defined territory. The protocol should be flexible to fit every specific scenario. The emergency network is hierarchic and is usually activated by first responders on the local level, as mentioned above. General recommendations for suspected biological threat are well known, along with institution-specific response plans, health care facilities readiness, principles of comprehensive communication and management networks [42] [43].

As known, WHO declared COVID-19 a Public Health Emergency of International Concern (PHEIC) on 30 January 2020 [44] and a pandemic on 11 March 2020 [45].

Italy declared the first patient positive for SARS-CoV-2 to the world on February 21, 2020, when a patient in critical condition with diagnosis of interstitial pneumonia of undetermined origine was tested for SARS-CoV-2 in Lombardy [46]. An immediate collection of available information about SARS-CoV-2 and evaluation of reliability of data sources have been a real fight of 2020.

The coded diagnosis ICD-10 and the first diagnostic criteria were introduced by WHO in March 25, 2020 [47], when the first Italian national "lockdown" was about to be ended (April 2nd, 2020).

However, there were multifocal burst-outs of SARS-CoV-2 globally present at that time [48] [49].

Table2. *General critical points of emergency response and management, emerged during and after Covid-19 pandemic. We worked with syndromic diagnosis of the infection by SARS-CoV-2 in the critical period in the winter 2019 – 2020, when the coded diagnosis has not been introduced yet. Noteworthy, the recovery phase draws from pre-threat and early epidemic phase management. The strategic gap between national and global level is evident. Recovery ought to lean against an adequate preparedness in order to make the future evolution of the society and resilience possible.*

Suspicion of potential biological threat and identification of biological agent	Preparedness and readiness epidemic/pandemic plan (outbreak response and prophylaxis plan); Epidemic intelligence; Syndromic surveillance versus astute observer; ED surveillance (for example syndromic diagnosis, critical patient rate, all causes mortality rate and critical patient mortality contextualized to the standards of the area); Public information;
Public information	Disinformation and misinformation lead to the uncontrollable behavior of the population, mistrust in the authorities;
Risk evaluation	Trigger of emergency response; Early delimitation of hot zones;
Predisposition and management of critical infrastructures and resources	Definition of the "bottleneck/s; Cooperation of all types of health facilities – both public and private, long-term facilities; Positivity rate vs hospital recovery rate vs critical patient rate; Needs of infected and non-infected patients; Healthcare for the population not affected by the emerging pathogen; ICU and general hospital beds availability;
ED	"Snapshot" and trend of the current epidemiologic situation; Overcrowding versus emergency management;
Territorial emergency system	Mediator between critical infrastructures and territory; First territorial triage; Analysis of territory data (OHCA, stroke, trauma …) and pre-hospital management;
Communication, epidemiology and statistics	Communication among HUBs and spokes, Provinces, Regions; Complex management of critical infrastructures; Coded diagnosis versus syndromic diagnosis;
Global Threat	Re-definition of the role of international institutions; Communication of relevant information;
Social countermeasures	Schools and social activities need particularly clear indications based on risk - benefit ratio.

Bio surveillance system is designed to recognize a potential biological threat in time, before the first manifestations are evident. As evidenced by WHO, in case of Covid-19 the interpretation of Influenza Like Illness (ILI) and Severe Acute Respiratory Infections (SARI) incidence was indicative of a respiratory disease epidemic in China in 2019, but they were not indicative of a new emerging pathogen or a pathogen different from known biological agents [50]. Early identification of biologic risk is of fundamental relevance to the public interest for the most effective tool against uncontrolled spread. Grounds on Event Based Surveillance (EBS) and Indicator Based Surveillance (IBS), which constitutes the so-called epidemic intelligence. IBS includes for example syndromic surveillance in Emergency Departments (EDs).

However, comprehensive WHO COVID-19 surveillance included basic actions as the use and adaptation of existing surveillance systems, laboratory testing or contact tracing. The resuscitated essential surveillance for Covid-19 was based on surveillance in the community, primary care, hospital-based, sentinel syndromic surveillance and mortality surveillance. Epidemiologic classification of transmission pattern categories and the risk of infection for the general population CT1 – CT4 (WHO 2020) were adapted and applied on management of Covid-19 [11].

In April 2020 the WHO published a dealing with COVID-19 strategy which bases on the worldwide cases reported during past months [51]. These practical guidance for strategic actions, were tailored to the local context, addressed to individuals (communities, governments, private companies) are based on prevention through the face and hand hygiene, on a proper respiratory etiquette, physical distancing, restrictions on travelling and holding gatherings, appropriate medical care and vaccination, etc. [52]. Interpretation of the rules is up to every signatory State.

The tight sequence of fourfold pandemic phases along with the interpandemic, alert, pandemic and transition phase, was previously considered aligned with the stages of the risk assessment: prevention – preparedness - response – recovery (PPRR) [53]. Covid-19 experience shows that the continuous burst-outs in various regions in different time, the biological characteristics of SARS-CoV-2, the peculiarities of every single national or regional context and global extension allow to apply these basic rules only partially and require a complex and more flexible approach. Standard protocols and emergency plans became one of the numerous possible scenarios.

The early delimitation of hot zones, one of the basic rules in biological threat management, became lacking in case of Covid-19, considered characteristics of SARS-CoV-2 and rapid diffusion worldwide.

Restrictive physical distancing measures combined with widespread testing and contact-tracing resulted to be effective in mitigation of the pandemic. Mathematic – physical modelling of epidemic trend confirmed the reliability of pandemic countermeasures adopted in Italy. For Italy Giordano et al proposed an eightfold infection stages epidemic model to get an effective control strategy. His SIDARTHE model is based on distinction of diagnosed and non-diagnosed individuals, because the first ones are usually isolated and much less likely spread infection [54]. If integrated to the planning of social, economic and production activities may result in an acceptable risk-management avoiding more restrictive measures as complete closures (lockdowns). Italian experience of complete lockdown in red zone and keeping opened elementary schools in “orange” zone is compatible with the fact, that the population in risk of transmission are children and seniors. The children in risk of transmission are mostly adolescents, whose activities may be planned and the school activity in presence alternated with cycles of distance learning.

Korean Coronavirus contact tracing study (2020) documented, that children of 10 – 19 years old resulted at high risk for transmitting respiratory viruses to household members, but not out of the house (43/231 children, 18.6%, CI 14.0–24.0). The adults resulted at risk of transmission of the virus: 60 – 69 years old 17%, 70 – 79 18%, >80 14,4%, tot. 11,8% in household. Out of the house the total risk of transmission fluctuated around 1% for children, 60 – 69 years old 2,9%, 70 – 79 4,8%, >80 4,6%, tot. 1,9% (CI 1,8-2,0) [55].

The complexity of the phenomenon and its dependence on social, cultural, political, economic context is contained in the statement “the pandemic is a “complex emergency” [56].

CONCLUSIONS

There are critical passages and points in every emergency system related to the specific social, economic, political, biological – medical context, as a complex emergency determines.

On the national level we may state that an astute observer activated the emergency network. We worked with terms syndromic diagnosis, critical patient rate, all causes mortality rate and critical patient mortality contextualized to the standards of the area.

Positivity rate versus hospital recovery rate versus critical patient rate define the category or grade of the emergency.

Needs of infected and non-infected patients were confronted. The population not affected by the virus resulted as important as the ill part of the population, determining indirectly shifts in emergency management.

The definition of the population at risk of transmission in every context became crucial and may differ from standard mitigation countermeasures.

Overcrowding and emergency management coexisted in certain time period and required different approaches.

The role of institutions in the position of the international mediator is about to be revisited.

The risk-benefit ratio and the availability of the resources becomes the first criteria, while absolute numbers became a historical issue.

Communication of relevant information remains a cardinal issue of the biological threat management and response.

The functional distress of the society affected by a threat may become one the criteria.

With sadness we note the unexpected passing of Prof. Fabrizio Fontana. We wish to acknowledge his invaluable contribution in our work.

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