

# Characteristics of the Biological/Bioterrorism Agent in the Context of the Covid-19 Pandemic

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### ABSTRACT

The ongoing Covid-19 pandemic, still with periodic outbreaks worldwide in 2022, made the terms biological agent, biological threat, bioterrorism, CBRNE event, biological weapon, and global biological risks more evident. While, they may overlap from certain points of view, they differ from the legal perspective. Historically, traditional biological agents and the ways in which they were used are well known. Biological threats of the last few decades, potential or effective, limited or worldwide, confirm the "evolution" of potential biological agent characteristics, supported by the changes in the dynamics of this type of event. The characteristics of biological agent go along with the complexity of the biological threat, as evidenced by the Covid-19 pandemic.

**Keywords:** Covid-19 pandemic, Biological agent, Biological threat, Bioterrorism, CBRNE event, Biological weapon, Global biological risks.

#### **BASIC TERMS**

The term biological agent is basically related to a few types of events. From a systematic point of view, the biological threat belongs to the group of the CBRNE events, classified as a terrorist act or a hazardous materials accident (HAZMAT), on the basis of the intention or accidentality of the event. Chemical. Biological, Radiological, Nuclear, and Explosive events are characterized by the uncontrolled release of chemicals, biological agents, or radioactive materials to the environment or explosions that cause widespread damage [1]. In the field of the biological threat classified as a CBRNE event, we talk about biological warfare agents, biological weapon hazards/risks, naturally occurring diseases, and toxins as causes.

Bioterrorism is defined as the planned and deliberate use of pathogenic strains of microorganisms such as bacteria, viruses, or their toxins to spread life-threatening diseases on a mass scale in order to devastate the population of an area [2] [3].

CBRNE events are much more frequent than global catastrophic risks (GCRs), the second major group of biological threats in terms of extension and impact [1].

Frequently cited examples of GCRs include nuclear war, climate change, and pandemics of naturally occurring or deliberately engineered pathogens [4] [5] [6] [7].

GCBRs are a subset of global catastrophic risks (GCRs). The Johns Hopkins Center for Health Security's working definition of global catastrophic biological risks (GCBRs): "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" [4]. We may say that this definition makes very close bioterrorism and GCBR in some cases. For example, H1N1 pandemic in 2009 or H5N1 epi-zoonotic in 2005- 2007 corresponds to the characteristics of GCBR, caused by potential bioterrorism agents [4].

In the field of biological weapons (BW), the primary target is the military, where we talk about a homogeneous population of healthy soldiers. The primary objective of BW is massive destruction; or disruption of the enemy forces [38].

Remaining in the field of the civil framework, we will not enter the "gray zone" or the lowintensity conflict [8] [9].

Bio crime implies to use of a biological agent to kill or make ill a single individual or a small group of individuals, motivated by revenge or economic gain through extortion [10].

### **A BIT OF HISTORY**

In ancient times, before the microbiological era, the methods were very raw, as contamination of water sources by fecal material, for example. In 1346 -1347 the Tartars catapulted the bodies of bubonic plague victims over the walls of the city of Kaffa to invade Crimea. The plague epidemic that followed forced the defenders to surrender. Some historians report that this was the cause of the epidemic of plague that swept across medieval Europe, killing 25 million persons [11].

The "traditional" bioterrorism agent anthrax, botulism, plague, and smallpox are four Class A agents of the modern era used during the Wars [12]. Tularemia, brucellosis, Q fever, viral hemorrhagic fevers, viral encephalitis, and disease associated with staphylococcal enterotoxin B [13] are the core of every biodefence list as well.

From the 1980s on, one example was offered by the Rajneesh cult, a religious group, which in 1984, intentionally contaminated salad bars with Salmonella typhimurium in various restaurants in Dalles, Oregon. This attack resulted in 751 cases and 45 hospitalizations [3]. Approximately 60% of all human diseases and 75% of all new and emerging infectious diseases are zoonotic in origin [14]. A recent example was foot and mouth disease, a naturally occurring disease in cattle, in the United Kingdom in 2001. The direct damage agriculture was followed by the to compromission of the food chain. Thus, we may remember, that the aim of agroterrorism is generally the secondary impact of terror and human health disruption.

#### CHARACTERISTICS OF BIOLOGICAL/ BIOTERRORISM AGENT

Three categories of bioterrorism agent, A, B, C are recognized [15].

Characteristics of bioterrorist agents, as reported in the past, might be: high morbidity and high lethality; highly infectious or highly toxic (low ID 50 or ICt50); suited for mass production and storage until delivery without loss of pathogenic potential; suited for methods aimed at wide area delivery, and hard to withstand the delivery process; relatively stable in the environment after dissemination for a period long enough to infect humans; BW agent genetically modified and/or suitable for weaponization process [16].

Today we talk about dried spores and genetically modified organisms causing acute respiratory failure in minute quantity via aerosol [4] [17], that almost seems to cause an inhalation injury.

The recent wakes up calls in the field of global catastrophic biological risk (GCBR) were considered outbreaks of pandemic influence, MERS, Ebola, and Zika [18]. Other global catastrophic risks were thought to origin from the natural world but or consequences of technologies or man-made. The targeted population threats involving an individual or a group of people with a shared genetic history, novel strains of known contagious pathogens, created deliberately with the goal to maintains high virulence (for es. H5N1) or adding respiratory transmissibility, global eradication of food sources by plant or animal pathogens, were reported by Schoch-Spana in 2017 [4].

Recently or in the proximal past SARS-CoV and MERS-CoV appeared and were studied. The SARS-CoV, beta corona virus, lineage B, caused an outbreak of severe respiratory disease in China during 2002–2003, spread to other countries in Asia, North America and Europe over 9 months (37 countries totally). 8273 cases were reported, with 775 deaths for a case fatality rate of 9%. Majority of cases and deaths occurred in China and Hong Kong. Mortality rate of the elderly was over 50% [19].

MERS-CoV was responsible for an on outbreak of severe respiratory disease in the Middle East since 2012 [20] [21] [22]. Clinical manifestations of MERS-CoV infection range from asymptomatic to severe pneumonia. Until December, 31 2015, a total of 1621 laboratory-confirmed infections have been reported, with 584 deaths (CFR = 36.0%) over 26 countries. The route of transmission from animals to humans is not fully understood. Dromedary camels are the major reservoir host for MERS-CoV and an animal source of infection in humans. Since 2012, 27 countries have reported cases of MERS, mostly in the Middle East [20] [21] [22] [23].

# SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS-2

In December 2019 a novel coronavirus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2 or 2019-nCoV) spread and was observed for the first time in Hubei province in China. Coronaviruses are a family of RNA viruses that typically cause mild respiratory disease in humans. A novel coronavirus was identified in Wuhan in December 2019. According to the current data of WHO, in June 2020 8,708,008 of infected and 461,715 deaths for Covid-19 were confirmed worldwide. As of 8 October, 2021 236.599.025 confirmed cases of COVID-19 and 4.831.486 deaths were reported. In January, 2022, 5.570.163 deaths and 340.543.962 confirmed cases were registered [24] [25].

Six corona viruses (CoVs) are known to infect humans: 229E, OC43, SARS-CoV, NL63, HKU1, and MERS-CoV. Many CoVs are simultaneously maintained in nature, allowing for genetic recombination, resulting in novel viruses. The genomic sequences obtained from early cases shared 79% sequence identity to the CoVs that caused severe acute respiratory syndrome (SARS CoV) in 2002–2003 in China and 96.2% sequence identity to RaTG13 (MN996532), a CoV sequence detected from a Rhinolophus affinis bat. [20] [26] [27].

In 2020 Segreto e Deigin presented the hypothesis that the chimeric genetic structure of SARS-CoV-2 and furin cleavage site of the virus might be the result of genetic manipula-

tion, both natural and artificial [8]. They reported that acquisition of both unique features by SARS CoV-2 simultaneously is less likely to be natural or caused only by cell/animal serial passage.

Many studies have reported the bats as natural reservoirs for potentially pathogenic SARSlike CoVs [20] [26] [27]. Some of these viruses can potentially directly infect humans [29], whereas others need to mutate their spike protein in order to effectively bind to the human angiotensin 1-converting enzyme 2 (hACE2) receptor and mediate virus entry. The furin 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 [29][30]. The ubiquitous expression of furin in different organs and tissues has conferred to SARS-CoV-2 the ability to infect organs usually invulnerable to other CoVs, leading to systemic infection.

Sirotkin discussed all above mentioned facts, pointed out the question of potential zoonotic jump and its interpretation in the contest of Nuremberg Code and the meaning of the Centre for Arms Control and Non-Proliferation [30]. However, some authors work with the hypothesis of a naturally occurring disease with unprecedented global impact [31].

According to the World Health Organization (WHO), the three main transmission routes, such as droplet and contact routes, airborne transmission and fecal and oral for COVID-19, have been identified.

The primary mechanism of transmission of SARS-CoV-2 is via infected respiratory droplets, by direct or indirect contact with nasal, conjunctival, oral or gastrointestinal mucosa. Transmission risk depends on factors contact pattern, such as environment, infectiousness of the host, and socioeconomic factors [32]. Morawska and Cao published the report underlining the airborne transmission of SARS-CoV-2 by aerosol droplets [33]. Experts in droplet dynamics and airflow in buildings confirm the hypothesis. Precautions indoor include increased ventilation rate, natural ventilation. avoiding air recirculation, minimizing the number of people sharing the same environment, and use of personal protective equipment (PPE), in particular masks and respirators.

SARS-CoV-2 is high priority a biological/bioterrorist agent of class A according to the US CDC. The class A these characteristics: presents easv dissemination, transmission from person to person, high mortality, potentially major impact on the health system, social disruption, special health preparedness [15].

One of the first estimate crude numbers of clinical case fatality rate for SARS-CoV-2 infection 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 [34]. Johns Hopkins University of Medicine reported in April 25, 2021 2,2% [35], Coronavirus disease 2019 case surveillance, United States published 5% in January 22–May 30, 2020.

The droplet and airborne transmission, incubation period of 5 - 6 days [32] and rapid global diffusion (in a couple of months) define a global threat with remarcable social, economic and political impact.

### COVID-19

The disease caused by SARS-CoV-2 is called COVID-19) [36]. About 40% of cases will experience mild disease, 40% will evolve into moderate disease including pneumonia, 15% of cases will lead to severe disease, and 5% of cases will end up in critical disease [32] [37] [38]. COVID-19 follows a biphasic pattern of illness that results from the combination of an early viral response phase and an inflammatory second phase, characterized by a "cytokine storm." Most of clinical presentations are mild, an influenza-like illness, which includes fever, cough, malaise, myalgia, headache, and taste and smell disturbance - rather than severe interstitial acute respiratory pneumonia, distress syndrome, respiratory failure, and death. Extra pulmonary manifestations may appear in all the organ systems, the most devastating and long term are cardiovascular and neurological disorders [32] [38].

## POST-ACUTE AND CHRONIC COVID-19 Syndrome

Similarly, to post-acute viral syndromes described in survivors of other virulent coronavirus epidemics, there are increasing reports of persistent and prolonged effects after acute COVID-19. Post-acute COVID-19 syndrome is characterized by persistent symptoms and/or delayed or long-term complications beyond 4 weeks from the onset of symptoms, concerning various organ systems [39].

Considered the gravity of symptoms and objective findings and re-admissions in hospital of discharged Covid-patients during the first waves of the pandemic in 2020 and 2021, it is clear that the care for COVID-19 patients does not conclude at the time of hospital discharge, and interdisciplinary cooperation is needed for comprehensive care of these patients in the outpatient setting.

Based on recent literature, it may be divided into two categories: subacute or ongoing symptomatic COVID-19, which includes symptoms and abnormalities present from 4-12 weeks beyond acute COVID-19; and chronic or post-COVID-19 syndrome, which symptoms and abnormalities includes persisting or present beyond 12 weeks of the onset of acute COVID-19 and not attributable to alternative diagnoses. All organ systems may be affected, probably the most serious include: thromboembolic events of all organ especially acute and system, chronic pulmonary thromboembolism, coronary thrombosis, stroke, lung fibrosis, neuropsychiatric manifestations, renal injury Pediatric inflammatory multisystem etc. syndrome temporally associated with SARS-CoV-2 (PIMS-TS) is an expression of devastating damage and invalidity of future generations in the contest of this pandemic [39].

Covid Stress Syndrome (CSS 2020) is acute and/or chronic neurological and neuropsychiatric manifestation of Covid-19 due to the passage of SARS-CoV-2 across the haemato-encephalic barrier. A severe form of the syndrome, characterized by clinically significant distress and impairment in functioning, is the COVID Stress Disorder, which is regarded as a pandemic-related adjustment disorder [40] [41].

The treatment of Covid-19 is principally symptomatic, such as Oxygen therapy, artificial ventilation, ECMO treatment, monoclonal antibodies and antiviral treatment. Vaccination was introduced in the autumn 2021.

## SOCIAL-ECONOMIC-BIOLOGICAL CONTEXT OF COVID-19 PANDEMIC

Any use of the biological agent is tightly related to the aim, primary and secondary impact, and target population. In case of natural disease, we could talk about the well-known epidemiologic triangle host – agent – environment. The interaction of host and the agent in the specific environment may lead to the disease.

However, the words fear, terror, panic, confusion, social and economic disruption, "far-reaching" psychological impact or economic changes figure in all the definitions mentioned above, in the definition of terrorism as well [16][42][43][44]. For instance, the anthrax attack ("Amerithrax") in the USA in 2001 was associated with only five deaths, but the social disruption and diversion of health and policing resources was massive [45].

Africa presented a different pattern of morbidity and mortality for Covid-19, which was and still is very low, considered population, geography, climate, medium age as reported by some authors already [46]. It is noteworthy to say that social and economic system and health care systems standards influence the possibility and decision to test the population and therefore the statistic morbidity and death rate for Covid-19. In this way many Covid-19 cases remain undiagnosed in Africa, however susceptibility of various continental populations has not been precisely studied until September 2021. Genetic predisposition and immune system adaptation might play an important role in receptor

presentation of any specific nation or population.

Observing what happened in countries with likely high and low Global Domestic Product, for example in USA and African countries in poverty, many political, social, organization considerations have emerged. The social aspects and the complexity of the Covid-19 emergency such as anti-Covid mitigation measures, lockdowns and stay-at-home order, country borders closure, "Infodemic" etc., in the contest of economic differences among the countries, have been described. Maniscalco used the term "complex emergency" [47].

The biological threat suggests to verify the association between number of hospital beds and Covid-19 mortality. Sen-Crowe B investigated global hospital bed (HB), acute care bed (ACB), and intensive care unit (ICU) bed capacity and determine any correlation between these hospital resources and COVID-19 mortality. In his study high-income regions had the highest mean number of ICU beds (12.79) and hospital beds (402.32) per 100,000 population; whereas upper middle-income regions had the highest mean number of ACBs (424.75) per 100,000. A weakly positive significant association was discovered between the number of ICU beds/100,000 population and COVID-19 mortality. No significant associations exist between the number of HBs or ACBs per 100,000 population and COVID-19 mortality [48] [49]. unexpectedly.

 Table1. Possible characteristics of biological/bioterrorist agent and impact.

Historical characteristics	<b>Recent characteristics of efficient</b>	SARS-CoV-2
of a BT/BW agent	biological/bioterrorist agent	
- "traditional" bioterrorist agents with known disease course and diagnostic and therapeutic procedure; - "4" agents Class A: anthrax, botulism, plague and smallpox;	<ul> <li>outbreaks of pandemic influence, MERS, Ebola, and Zika [18];</li> <li>consequences of powerful man-made technologies</li> <li>target population may be a group of individuals or people with a shared genetic history</li> </ul>	<ul> <li>unknown or partially known agent;</li> <li>result of genetic manipulation, both natural and artificial [29];</li> <li>long-term sequele of the disease;</li> <li>multifocal burst-outs globally in the moment of momential</li> </ul>
<ul> <li>tularemia, brucellosis, Q</li> <li>fever, viral hemorrhagic</li> <li>fevers, viral encephalitis,</li> <li>disease associated with</li> <li>staphylococcal enterotoxin</li> <li>B [13];</li> <li>specific technical</li> <li>description of BT/BW [10];</li> </ul>	<ul> <li>novel strains of known contagious pathogens, created deliberately with the goal to maintains high virulence (for es. H5N1) or adding respiratory transmissibility</li> <li>multiresistant bacteria</li> <li>global eradication of food sources by plant or animal pathogens [4]; zoonotic infection remains one of the more frequent threats</li> </ul>	in the moment of recognition (global extension); - CBRNE event may become a GCBR in a very short time - non-diagnosed population becomes a critical issue in the emergency management
- the event causes a direct damage, which remains physically in a delimited area	- direct damage becomes less significant, the distant break-outs are present	<ul><li>secondary and long-term impact is significant;</li><li>"complex emergency"</li></ul>

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Infodemic, overabundance of information, was treated by WHO. Term "infodemic," as reported Rothkopf in Washington Post in 2003: An "infodemic" is an overabundance of information – some accurate and some not – that occurs during an epidemic [50]. The "infodemic" was confirmed by WHO Director-General Tedros Adhanom Ghebreyesus on 15 February 2020 [51].

Morover, the mathematic – physical modelling of the epidemic trend (Italy, 2020), dedicated to the efficacy of the restrictive pandemic countermeasures and widespread testing, pointed out that the portion of the population mostly in risk of transmission were nondiagnosed individuals, because they are not usually isolated and more likely spread infection [52].

#### DISCUSSION

Covid-19 pandemic dynamics show the remarkable transformation of the concept of the biological threat. Both pandemics and terrorist attacks are widely considered to be low - probability and high-impact events [53] [54], which are always a management challenge for the lack of historical records or comparable data [55]. In the case of naturally occurring-disease. the unreadiness and unpreparedness to face natural evolution of terrestrial fauna may lead to global shifts. A slowly evolving phenomenon with insidious onset may by-pass emergency response in the first phase.

The real "3D impact" on the population may present as undifferentiated: a biological agent causes a disease in the sensitive population, which is supposed to be diagnosed and treated. There are economic, social, and political changes supported by psychological and diplomatic mechanisms always present. In this article, we exalt the civil framework and context, considering that the natural and artificial emergence of the agent is overlapping.

#### CONCLUSIONS

SARS-CoV-2 characteristics confirm the remarkable transformation of the concept of the biological threat. The Biological agent causing a "below-threshold" event or risk, very early global diffusion, leading to the difficult and complex emergency management, failure of emergency response plans and health care systems, social, political and economic disruption is a high priority biological/

bioterrorism agent of class A. The global social, political, economic, and human impact is unprecedented.

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