



Lessons learned from 2001–2021 – from the bioterrorism to the pandemic era

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Abstract

Introduction and Objective. The aim of the study was to analyze available literature on the development of biological warfare and combating the SARS CoV-2 pandemic. Against the background of contemporary threats from biological factors, the strengths and weaknesses of response in the event of a bioterrorist attack during the ongoing COVID-19 pandemic have been identified. The scope and importance of international cooperation in the fight against the pandemic is assessed.

Review methods. The more important literature on bioterrorism, biological weapons and the COVID-19 pandemic, both from earlier work and recent publications, was analyzed, emphasizing new threats and adequate defence against them.

Brief description of the state of knowledge. The bio-warfare threat and the current COVID 19 pandemic that has hit mankind on a global scale has clearly shown how dangerous biological agents are and what effects they can cause, negatively affecting every sphere of human activity with catastrophic consequences. Data on examples of bioterrorist attacks carried out and research on the development of biological weapons and methods of combating pandemic COVID-19, were reviewed. New threats related to technological development, including those resulting from genetic manipulation, biosynthesis, and modern means of delivery, are pointed out. Attention has been paid to the implications of controlling the proliferation of biological weapons and the issues of international cooperation in the fight against bioterrorism and the COVID-19 pandemic.

Summary. The lesson learned clearly demonstrates the weakness of states in responding to such threats. The risks of uncontrolled scientific advances are still underestimated. Appropriate international control measures must be taken urgently to prepare for new pandemics, bioterrorist attacks, and the possibility of using modern biological weapons.

Key words

bioterrorism, biological weapon, pandemia, public health, healthcare system, COVID-19, biosecurity

INTRODUCTION

In the past, biological threats were an important factor hindering the advance of civilisations and limiting the prosperity of societies. Great epidemics of incurable infectious diseases caused the collapse of many societies, shaped the course of wars, and determined the progress humanity. The scientific progress of the 19th and 20th centuries in discovering the real causes of their occurrence and in their diagnosis, prevention, treatment and control, was a milestone for modern civilization. The achievements in microbiology and vaccinology stand alongside the invention of the steam engine and exploitation of electricity as the instigators of rapid demographic growth concomitant with industrial and economic development. Paradoxically, in the times of the great wars of the 20th century, the industrial and scientific revolution made it possible to use new discoveries in armed conflicts. In an analogous case to that of the chemical industry and chemical weapons, the industrial-scale production of drugs and vaccines has made it possible to create one of the least humane weapons of mass destruction in the modern biological armoury.

From biological weapons to bioterrorism [1, 2, 3, 4]. Since the dawn of history, man has sought to find effective means and methods of neutralizing an enemy. History chronicles attempts to poison drinking water, including by throwing dead animals into it, or using the corpses of people who had died of infectious diseases. These were catapulted over the walls of defended cities and strongholds to cause disease among their defenders. The Tatars used this method in 1346 during the siege of Kaffa, causing a plague epidemic which spread into Europe and caused a huge loss of life. In the 16th century, when fighting the Incas in South America, Francisco Pizarro gave the Indians blankets infected with the smallpox virus, which decimated their population. Two hundred years later, in 1763, the English Captain Simeon Ecuyer used smallpox-infected blankets against hostile tribes in North America, causing an epidemic in the Ohio River Valley.

Only at the beginning of the 20th century had knowledge advanced sufficiently for the first attempts to make to create effective biological weapons and use them in a targeted way. Biological weapons can be directed against humans, causing epidemics; animals, triggering epizootics; and plants, seeding epiphytotics. In addition, a number of agents cause disease in both humans and animals (zoonoses). During the First World War, Germany infected cattle and sheep with spores of *Bacillus anthracis*, as well as infecting horses

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and mules destined for the Allied powers with *Burkholderia mallei*. The latter caused both animal losses and human deaths. Despite the international ban on the use of biological weapons [5], from the 1930s until the end of World War II, research programmes were conducted in several countries, the most developed having been conducted by the Japanese under the direction of General Shiro Ishii. In the Japanese programme, the secret facilities known as Unit 731 and Unit 100 produced anthrax spores, *Yersinia pestis*, *Vibrio cholera*, *Neisseria meningitidis*, *Shigella* sp., and *Burkholderia mallei*. The Japanese were the first to master the production of ceramic biological bombs and use aircraft to spray biological aerosols or drop infected fleas and rodents. The effectiveness of the new weapon was tested on convicts or prisoners-of-war, and the weapon was used on a larger scale against the Chinese population which caused local epidemics. It is estimated that about 10,000 prisoners died as a result of these criminal experiments. In the 1940s and later, the USA, UK, and USSR conducted research on biological weapons [6]. As a result of the US biological weapons development programme at Camp Detrick (Maryland) and other places, a huge arsenal was produced comprising aerial bombs, artillery ammunition and warheads containing *B. anthracis*, botulinum toxin, *Francisella tularensis*, *Brucella melitensis*, *Brucella suis*, *Coxiella burnetii*, staphylococcal enterotoxin B, or the Venezuelan encephalitis virus as biological agents. Only in the time of President Nixon, specifically in the years 1971–73, did the process of disarmament and destruction of biological weapons begin, and Fort Detrick (now the US Army Medical Research Institute of Infectious Diseases) was switched to research of a defensive nature. Similarly, under the supervision of the microbiology at Porton Down in Wiltshire, the UK carried out experiments in 1942 on Gruinard, a small island off the north-west coast of Scotland, using *B. anthracis* spores and testing anthrax bombs on sheep. All the animals died, the disease spread quickly. Due to the devastating impact on the environment, the study was terminated and the island remained contaminated for decades and required painstaking decontamination [7]. No one was permitted to visit the island until 1990.

The Biological and Toxin Weapons Convention drawn up in 1972 on the prohibition of the development, production and storage of biological weapons, signed and ratified by most countries and which came into force in 1975, did not, however, protect the world from biological threats, [8]. While the US and the UK stopped conducting experiments on biological weapons, the third most important signatory to the convention, the USSR, continued to work on these weapons, as revealed by a random incident in Sverdlovsk in 1979. The accident was the release from military facilities of 100 g of *Bacillus anthracis* endospores, as a result of which officially 96 people fell ill (with the pulmonary form of anthrax), of whom 66 died (local sources reported 105 deaths). According to Ken Alibek [9], former Deputy Director of the Soviet Biopreparat All-Union Science Production Association which was ostensibly a civilian programme employing tens of thousands of specialists, including microbiologists, geneticists, bioengineers and technicians, participated in the Soviet research on biological weapons, involving dozens of scientific and production institutions and several testing and training grounds. Tons of biological warfare agents were produced at the Biopreparat facilities. In addition to the agents also available to opponents on the other side of the Iron

Curtain, the decision was made to also use smallpox, which casts doubt on the intentions of the Soviet Union in having been the initiator of the programme for the effective global eradication of this disease at the World Health Organization (WHO). The biological agents were placed in modern means of delivery – bombs, rockets (especially ballistic variants) and missiles. More threateningly, to achieve the strategic goals, strains of microorganisms were used which after genetic modification, became resistant to known antibiotics while showing the ability to break through immunity in previously immunised people. According to Alibek, chimeric organisms were also used.

The tense international situation which prevailed after the discovery of the violation of the Convention by Russia calmed down considerably after the announcement by President Yeltsin in 1992 of his decree terminating the biological weapons research programme. Doubts existed, however, and were discussed for many years [10]. Currently, the US State Department regards the Russian Federation as a state with an active biological weapons programme [11]. Similarly, in the Middle East, Iraq conducted research and development from 1970–1991 on *B. anthracis*, botulinum toxin, ricin, aflatoxin, *Vibrio cholera* and enteroviruses. Three of them were used as weaponised agents: *B. anthracis* spores, botulinum toxin and aflatoxin. A total of 200 R 400 bombs were produced and 25 SCUD warheads were armed. For the safety of American troops during the first Gulf War, the USA vaccinated 150,000 soldiers against anthrax and 8,000 against botulinum toxin. A stock of 30 million 500 mg doses of ciprofloxacin was accumulated, which allowed 500,000 soldiers to be treated within a month.

Selected cases of bioterrorism attacks. In 1984, a bioterrorist attack was reported in the Dalles, a city in Oregon State, US, carried out by the Rajneeshee sect, where *Salmonella typhimurium* was used in salad bars and infected 751 people, of whom 45 were hospitalised. The Japanese Aum Shinrikyo (Supreme Truth) sect carried out unsuccessful attacks in Tokyo in 1993 using *B. anthracis* and botulinum toxin. In retrospective investigation, it was shown that the failure was due to the use of the vaccine strain of *B. anthracis* not containing the plasmid pXO2, the presence of which is a condition for the full virulence [12]. This sect tried to obtain strains of the Ebola haemorrhagic fever virus during its epidemic in Zaire in 1992 for bioterrorist purposes.

In 2001, postal attacks with *B. anthracis* spores in envelopes were carried out in the United States which evoked a shocked reaction around the world. The attacks led to 22 people falling ill with anthrax, of whom 5 died of the pulmonary form, and more than 30,000 people were treated with antibiotic therapy. The bioterrorist attack caused chaos and outbreaks of panic throughout the United States, caused changes in social behaviour, and people isolating themselves from others. It also had serious negative economic consequences, e.g. through the costs of preventing anthrax, including the expense of disinfection of contaminated buildings which amounted to more than a billion dollars. These attacks showed the whole world the possible consequences of the use of an invisible weapon, i.e. biological agents for terrorist purposes. Almost all countries, including Poland, were and remain unprepared for this type of danger, which will be analysed below.

Biological agents – risk analysis and risk update. The classic lists of biological agents that can be used for bioterrorist purposes or as biological weapons have been compiled by the United States Army Medical Research Institute for Infectious Diseases (USAMRIID) and the American Centers for Disease Control and Prevention (CDC). Initially, 12 pathogens (*‘the Dirty Dozen’*), were listed in the USAMRIID ‘Blue Book’ – the Medical Management of Biological Casualties. In contrast, the CDC groups biological factors in three panels, A, B and C, according to the scale of the threat to human health.

Category A poses the greatest threat and includes pathogens that pose a high-level threat to national security because of their contagiousness and transmissibility, high mortality and negative impact on society consequent on their use. This impact manifests through panic and the need to devote resources to the organisation of countermeasures and preventive measures. This category includes: *B. anthracis*; *F. tularensis*; *Y. pestis*; botulinum toxin; smallpox virus (*Poxvirus variolae*); haemorrhagic fever viruses, including the *Lassa* (LASV), *Junin* (JUNV), *Machupo* (MACV), *Guanarito* (GTOV) and *Sabiá* (SABV) arenaviruses; the *Ebola* and *Marburg* filoviruses; and *nairovirus* (Crimean-Congo haemorrhagic fever virus).

Category B includes pathogens that pose a moderate threat due to their average infectivity and transmissibility, and average morbidity and mortality rates. These agents necessitate improvements in diagnostic capabilities and enhanced disease surveillance. They are: *Brucella* spp., Epsilon toxin (*Clostridium perfringens*), foodborne pathogens (*Salmonella* spp., *Escherichia coli* O157:H7, *Shigella* spp.), *Burkholderia mallei*, *Burkholderia pseudomallei*, *Chlamydia psittaci*, *C. burnetii*, *Ricinus communis* toxin, staphylococcal enterotoxin B, *Rickettsia prowazekii*, encephalitis viruses (alphaviruses, such as Western and Eastern equine encephalitis virus, Venezuelan equine encephalitis virus), and waterborne pathogens (*Vibrio cholerae* and *Cryptosporidium parvum*).

Category C includes emerging pathogens which, because of their availability, ease of production and distribution, in the future may be weaponised for mass distribution and potential for high morbidity, mortality, and impacts on health impacts. These viruses include the Hanta virus, identified in 1993 in the USA; Hendra virus, first identified in 1995 in Australia, and Nipah virus, first identified in 1999 in Malaysia.

After USAMRIID and the CDC had drawn up their lists, other international bodies adapted and created additional indicative list and checklists which extended our knowledge of the subject, and added more possible biological agents [13]. These lists include a variety of biological weapons of mass destruction (WMD) factors, from the classic initial list of 12 to over 30 [14]. A comparative matrix of different lists of pathogens by type of threat is presented in the cited literature. Currently, considering natural hazards, and due to the widespread use of effective antibiotics against bacteria, viruses have become the greatest threat, both in the context of defence against WM, as well as the protection of public health. For example, the most recent European Union (EU) list includes factors such as SARS, MERS, Hendra paramyxovirus, Monkeypox virus, West Nile virus, and the highly pathogenic influenza A H5 and H7 viruses, which are not on the classic list of the Centers for Disease Control (CDC).

Sources of modern threats. Totalitarian or undemocratic states are the main source of modern bioterrorist threats as the sponsors of terrorism and certain terrorist organisations. According to a report by the US State Department of April 2021, the Russian Federation is adjudged to have a biological weapons development programmes, and North Korea, Iran and China are also suspected of the same. Al-Qaeda has long been interested in biological agents. Instructions found in the Tora-Bora caves in Afghanistan concerning the methods of production and use of *B. anthracis* endospores and ricin testify to this. There are documented cases of the discovery of ricin with Al-Qaeda suspects in London; ricin is an extremely dangerous toxin, for which there is still no effective treatment. It was reported that infiltration attempts were made in the UK by more than a hundred Arab volunteers to undertake doctoral studies to gain knowledge, experience and ‘sensitive’ reagents.

The deaths in 2009 of 40 terrorists from plague in Algeria caused widespread consternation because these deaths were not the result of natural infection, but through an ‘accident in the workplace’ as a result of experiments with *Y. pestis* [15]. Al-Qaeda prepared terrorist suicide attacks against NATO troops by sufferers of certain infectious diseases (HIV, smallpox, and Ebola). The interest of the Islamic State (ISIS) in weapons of mass destruction, including biological weapons, was evidenced by data obtained from more than 36,000 contained in the laptop of one of ISIS jihadists.

The risks of smallpox virus. Smallpox (*variola vera*) is one of the most dangerous diseases in the history of mankind and sowed devastation globally for centuries, but was eradicated on 8 May 1980, thanks to the World Health Organisation (WHO) and the conjoined efforts of all nations. Countries which possessed the virus strains were obliged to destroy them, with the exception of two selected laboratories in the USA and Russia.

Gradually, preventive vaccinations were also discontinued worldwide which, over time, induced the vulnerability of mankind to smallpox. This vulnerability introduces the threat of a smallpox agent being used as a highly effective biological weapon. Intelligence indicates that some countries may illegally possess virulent strains of the smallpox virus (e.g. North Korea, which continues to vaccinate its citizens). The international community responded to the threat by organising the 2001 ‘Dark Winter’ and 2005 ‘Atlantic Storm’ simulation exercises. The latter was conducted with the participation of former prime ministers of several European countries under the direction of US Secretary of State, Madeleine Albright. The exercises showed the ineffectiveness of the countries of the world in locating the origin of the smallpox virus and stopping it, which led to a virtual global pandemic claiming an barely conceivable or estimable number of victims. The simulated pandemic ended with a permanent global endemism, that is, the re-conquest of the earth by *Poxvirus variolae* – smallpox. The exercise showed a severe shortage of global stocks of vaccine, difficulties in reproducing it, and an understandable reluctance on the part of individual countries to share their meagre stocks. The understandable concern of the American public and the large-scale interdisciplinary organisational, legislative and scientific action taken by the American authorities were discussed by Dr. Sabina Łysoń in her comprehensive doctoral dissertation [16]. Globally (including in Poland),

intensive efforts have been made to develop a new vaccine against smallpox and to stockpile it in proportion to the population. Currently, Poland has the Jynneos vaccine against smallpox and monkeypox, and in 2021, the US Food & Drug Administration approved the drug brincidofovir (Tembexa).

Biotechnology and bioengineering-- perception of new risks. The progress in recent decades in the field of molecular biology has fostered the dynamic development of the biotechnology industry, thanks to which a number of products can be conceived and developed that can solve the strategic needs of mankind, such as the production of medicines and food. However, biotechnology used detrimentally, e.g. by terrorist organisations and States supporting terrorism, or in breach of international conventions, can also pose huge risks for humanity. Through biotechnology it is possible to produce ideal biological agents for military or bioterrorist use, their propagation, modelling of their resistance to environmental factors, and the raising of their virulence is becoming ever easier. The Ad Hoc Group for Medical Research and the WHO published the criteria for such an 'ideal' biological weapon in 11 points, such as: high pathogenic efficacy, low cost of production, low infectious/toxic doses, difficulties in detection (e.g. because of genetic modification), the non-existence of prophylaxis or its low effectiveness, persistence in the environment, etc. It has become possible to modify various characteristics of microorganisms, so as to influence the course and symptoms of the diseases they cause. Deep modifications in the genome of microorganisms can cause changes in gene expression, forming mutants with new genotypic and phenotypic characteristics. The mutations can affect the composition and production of exo- and endotoxins, etc., to impart hitherto unknown but potentially dangerous properties to them. Modified microorganisms may transpire to be able to weaken the body's defences and/or break down its immune system, or conversely to stimulate its undesirable over-reaction, for example, by triggering a cytokine cascade or mechanisms of autoimmunity. Microorganisms resistant to modern therapies are created in these ways.

Scientists' curiosity to learn how to reshape nature, coupled with their openness in sharing research results and a desire to be noticed, often seems to be a sin of naivety that can lead to an uncontrolled transfer of knowledge and the proliferation of biological weapons. Moreover, as demonstrated by the COVID-19 pandemic, a line that had hitherto existed has been blurred: the line between the deliberate manufacture of agents of biological warfare and bioterrorism in bad faith and the genetic engineering of microorganisms for the declared purposes of making progress in their diagnosis and producing more effective vaccines. In this context, the term 'gain of function' has taken on an ambiguous, if not sinister, character.

Monitoring the directions in which knowledge is expanding, the results which are published and the possession of dual-use agents has become an important area of action in particular countries in the sphere of 'biosecurity' in the broad sense [17]. Models for 'experiments of concern' are included in the Fink Report of 2004 by the US National Research Council which designates as 'experiments of concern' such experiments that: define methods of making pathogens withstand hitherto effective vaccinations; introduce characteristics of resistance to antibiotics or antiviral agents; increase

virulence or reversion; increase the transmissibility of the pathogen; broaden the range of hosts; modify the characteristics that enable a pathogen's detection; and indicate the methodology for preparing biological agents for direct use as biological weapons [18].

In 2001, Australian researchers [19] obtained a strain of mousepox – mouse ectromelia virus, provided with a gene expressing IL-4 interleukin as a result of genetic manipulation. This strain unexpectedly overcame the insusceptibility of previously immunised mice, which indicated the existence of a pathway to modify other viruses, including smallpox. Making such changes and similar manipulations to the smallpox virus (e.g. the creation in Russia of an Ebola-poxvirus hybrid) and publishing how it was done, could bring catastrophic consequences for humanity. Another example of ill-considered research is that on the molecular basis of the complement system inhibition in smallpox viruses and the *Vaccinia virus*. The precise description of the mechanism in these viruses for regulation of this system could be used both to develop new methods of treating smallpox, and to increase the pathogenicity of the harmless *Vaccinia virus*. The possibility of pneumonic plague in rats by aerosol infection has been demonstrated and the kinetics of this infection have been shown [20].

In 1993–2002, an example of groundbreaking experiments opening up new possibilities in synthetic biology was made with the *in vitro* synthesis of polio virus only on the basis of a genetic sequence [21]. Since then, genetic information has become sufficient, as knowledge of complete genome sequences, to reproduce a number of biological agents under laboratory conditions. The regimen for controlling the possession of an agent has also been extended to include access to information on its synthesis.

As a result of genetic manipulations, hypervirulent strains were obtained of *Mycobacterium tuberculosis* [22] and *Leishmania major* [23]. A modified Legionella with a programmed new ability to express myelin after infection can stimulate the production of antibodies, thus triggering a demyelination process in the body, leading to paralysis and death [24]. Other studies focus on near-forgotten pathogens known in the past for their high virulence. Their re-synthesis is also a potential threat to the biological security of the world although, on the other hand, as demonstrated in the case of the Spanish influenza virus H5N1, the isolation of the virus from the remains of people buried in permafrost in Alaska and Spitsbergen and its sequencing gleaned the knowledge of the cause of the high mortality which followed this disease in the past [25]. In 1918–1919, 50–100 million people died as a result of the Spanish influenza pandemic, while in Poland the number of deaths was estimated at 200–300,000 [26].

Advances in the knowledge and techniques of nanotechnology, proteonomics, nanomaterials, polymers, liposomes and artificial intelligence do not only drive progress in rapid defensive diagnostics and the production of completely new types of vaccines, e.g. mRNA vaccines against COVID-19, or the reverse vaccinology method which has resulted in a vaccine conferring immunity against meningococcal group B after many years of research. These advances also bring to light new dangers in their enabling the production of organisms with improved characteristics which render them more useful for carrying out an effective attack.

In addition to bioengineering methods, further opportunities are created by the development of technology for the manufacture of structural components and the transport of biological weapons. Through 3D printing technology, it is possible to produce the parts for apparatus suitable for the release of biological agents, such as heads and atomisers for the production of biological aerosols [27]. The simplicity of project transfer and component manufacturing makes the issue of accessibility to technology impossible to incorporate into non-proliferation regimens. Bio-print technology is a threat because it is capable of printing biological elements using 3D bioprinters [28], similar to the development of remote and autonomous systems. Terrorist groups and States producing biological weapons are constantly acquiring new capabilities, some of which are gained by using drones capable of carrying biological payloads over long distance, and accurately hitting targets, e.g. through unmanned aerial vehicles (UAVs) [29]. They are capable of carrying biological charges over a distance of about 150 km, and are difficult to detect and neutralise.

Epidemics as natural phenomena and events invoked by man. Distinguishing between epidemics arising from natural causes and those brought about by human activity – either intentionally (bioterrorism) or through thoughtlessness (Sverdlovsk) – is often very difficult. Examples are the difficulties in detecting the perpetrator of the anthrax attacks in the USA, and the determination of the causes of mass food poisoning in The Dalles in the USA in 1984, only after the confession of the ‘repentant’ perpetrator. Some etiological, clinical and epidemiological signs may indicate a bioterrorist source of an epidemic: an atypical course of the epidemic for the given pathogen and its disease, atypical features of the particular microbe (e.g. multi-drug resistance, modification of the capsule, hybrids, etc.), an atypical infectious dose or an unusual route of the spread of the disease. As mentioned, the distinction between natural and induced epidemics, as a rule, remains very difficult. These problems were presented brilliantly by US Army epidemiologists [30], citing, *inter alia*, 11 warning signs indicating the unusual nature of an event and sensitising observers to possible unnatural causes of the phenomena:

- 1) highly unusual events with a large number of victims, especially when it is difficult to detect the cause with rational deduction, are to be strongly suspected of being intentional acts. Examples are the afore-mentioned salmonellosis in a salad bar in The Dalles and the anthrax epidemic in Sverdlovsk which, although not caused by deliberate action, was the result of the deliberate production of biological weapons;
- 2) unexpectedly high morbidity or mortality suggest the use of a biological agent with unusual properties and deliberately modified (e.g. with increased pathogenicity, multi-drug resistance, etc.), or one spread in a way unusual for the specific pathogen. Examples are the anthrax epidemic in Sverdlovsk and cases of pulmonary anthrax in recipients of the ‘anthrax letters’ in the USA;
- 3) an atypical disease;
- 4) an epidemic with a point source: e.g. the biological weapons factory in Sverdlovsk;
- 5) parallel epidemics; terrorists can release the same pathogen sequentially or simultaneously in different places;
- 6) a lower percentage of cases in protected persons, e.g. in vaccinated risk groups and/or in persons who are in buildings equipped with air filtration systems or using individual respiratory protective equipment, gives rise to suspicion that a biological agent was sprayed in a particular area;
- 7) dead animals: disease and/or animal deaths are a very sensitive early harbinger of an impending threat to humans – rat deaths foreshadow epidemics of bubonic plague or tularaemia; the deaths of sheep located downwind of biological weapons facilities in Sverdlovsk are another example; also the deaths of urban crows and exotic birds at the New York Zoo were the first signal of West Nile fever having been brought to the USA where hitherto it had been unknown;
- 8) reverse pattern of propagation – in the case of naturally-spreading zoonoses, disease manifestation in animals (and deaths of animals) precede human morbidity (e.g. in plague and tularaemia outbreaks); situations where animal and human diseases have occurred at the same time, and particularly, situations where human disease has preceded animal disease, should be suspected strongly of being disease spread unnaturally;
- 9) atypical forms of the disease associated with an atypical route of infection (e.g. aerosol infection with syphilis), a dose not encountered in natural infection, or the use of a modified infectious agent (e.g. a multidrug-resistant bacterium or even a virus hybrid);
- 10) a cone-shaped infection map determined by the wind; if the disease cases are plotted on a map, taking into account time and physiographical phenomena, if they form a regular triangle shape fanning out in the direction of the wind, there is a high probability of the microbe having been spread in the form of aerosol or dust. In the case of the anthrax epidemic in Sverdlovsk, such plot data was key evidence of aerogenic infection. The causes of such an epidemic can also be natural and testify to the high pathogenicity of agents which infect their hosts’ respiratory tract, such as *C. burnetii* (it has been shown that 1–2 cells of this pathogen can cause an infection when inhaled). The characteristics of the spread of biological contamination and their precise quantitative measurements are covered by NATO standards (STANAG ATP-45) [31];
- 11) direct evidence – the perpetrator deliberately leaves a trail; the ‘anthrax letters’ in the USA in 2001 are an example.

Differentiation between natural epidemics and those caused intentionally can be very difficult; however, it is possible using the appropriate methodology. From October 1999 until 30 June 2000, a tularaemia epidemic broke out in Kosovo, former Yugoslavia, which was then embroiled in a civil war. The fundamental question then was whether this was a natural epidemic in an environment with endemic tularaemia and devastated by war, or an epidemic caused by the introduction of strains of *F. tularensis* as a bioterrorist agent. A number of data supported both possibilities. Extensive interdisciplinary research showed that the outbreak had been caused naturally. The military epidemiologists Grunow and Finke, who were in the region where outbreak took place, exploited the experience they gained at the time and developed a quantitative tool for epidemiological analysis to confirm and

identify or exclude biological weapons as a factor causing epidemics of atypical infectious diseases [32]. The analysis by Grunow and Finke, and the criteria they created, proved to be very helpful in epidemiological investigation and are widely used in epidemiology as the classic scheme.

Means of conducting an attack. An intentional event such as a biological weapon attack can be staged in a variety of ways. The most dangerous is the biological weapon attack carried out by air (aerogenically, especially through aerosols and dust) on mass targets such as urban agglomerations. The extent of the harm caused, which is potentially the illnesses and deaths of hundreds or even thousands of people in a short time post-attack, depends on a number of factors, which are listed here only synoptically, referring to the sources [1, 2, 30, 31, 33].

Parameters, method of release and amount of agent used (attack scale):

- dose and presentation (liquid, powder or lyophilisate, infected animals such as insects, aerosol). The most 'effective' is an aerosol with a size of less than 5 µm, due to its reaching the lower respiratory tract;
- direct generators (agricultural atomisers and spraying machines, explosives), or additional means of delivery over longer distance – ballistic missiles or artillery ammunition, drones, aircraft, including, for example, agricultural and fire fighting equipment;
- the effectiveness of a biological attack depends on a number of factors, related both to the conditions of the attack (e.g. strength and direction of the wind, terrain, temperature, humidity and vertical stability of the air), as well as related to the protection of the exposed population (active and passive).

The type of pathogen used plays a crucial role. A number of pathogenic characteristics of the microorganism, including the basic R0 reproductive ratio/number, determine its effectiveness in inflicting disease. According to WHO estimates, the airborne spread of 50 kg of a virulent microbe across a city of five million would result in the following impacts, depending on the biological agent used [34]:

- *Yersinia pestis*: 150,000 cases, 36,000 deaths;
- *Francisella tularensis*: 250,000 cases, 19,000 deaths;
- *Bacillus anthracis*: 2,500,000 cases, 100,000 deaths;
- botulinum toxin: to contaminate 100 km² and achieve a population mortality rate of up to 50%, 80 kg of toxin would have to be used.

More precise predictions of the possible consequences of a biological attack are the subject of studies conducted worldwide, including in Poland [33]. In the Armed Forces of the Republic of Poland and its civil defence structure, a procedure applies based on the NATO standardisation agreement (STANAG) according to the ATP-45D methodology, which includes four types of classification of biological contamination (P, Q, R, and S) [31, 33]. It is essential to be able to detect an aerosol attack away from the target and to continuously monitor biological hazards in urban agglomerations (e.g. the BioWatch system in the USA). The key to minimising the effects of the attack are the population on whom protection is actively conferred (in cases of diseases, drugs and which are termed 'non-pharmacological protective measures' (individual and collective), training of the appropriate healthcare services in

the first line for vaccine-preventable diseases, an appropriate critical care infrastructure provided by the State, adequate to the number of inhabitants of the whole society.

The cost of the *Francisella tularensis* attack described above was estimated at \$5.4 billion per 100,000 people exposed, and that of the *Bacillus anthracis* at \$26.2 billion [35]; however, it is not only the consequences of an attack which deliver a heavy financial impact. Similarly, the preparation of monitoring and defence systems for the public and the health system is a very costly and time-consuming undertaking. The anthrax attacks in 2001 which showed how many States were unprepared to respond to this threat. To some extent, the reason for nations having been caught napping was the 1972 Convention which prohibited the signatories from producing, storing or using biological weapons. Unfortunately, it was not foreseen that the commitments would endure only on paper. During the anthrax attacks in the USA, diagnostic laboratories quickly lost their regular throughput capacity because of the huge amounts of samples for testing, and the lengthy waiting time for results. Similarly, pharmacies quickly sold out of antibiotics and disinfectants, and protective equipment were in short supply, which resulted in mass panic. Thanks to the provisions of the NATO summit in Prague, preparations for anthrax attacks were quickly launched in individual countries within the framework of the alliance. These preparations began with the replenishment of stores of protective equipment, and continued with the introduction of new field and laboratory diagnostic methods based on the new-for-the-time real-time PCR method, the development of systems for rapid detection of contamination of shipments, e.g. in post offices, the implementation of a system of laboratory examination of samples escalating through different levels of authority (e.g. the Reference Laboratory Network), the initiation of research on new vaccines and therapeutics, and the allocation of considerable resources for research on *B. anthracis*, etc. Systems for monitoring biological threats on an international scale have been introduced by the EU, WHO and NATO.

COVID-19 Pandemic – support from international institutions. In the autumn of 2019, the world was taken by surprise by a new threat – a pandemic of an acute infectious disease, later called COVID-19, caused by a coronavirus. Initially, the world passively watched the outbreak in the city of Wuhan in China (PRC), populated by 11 million people and home to one of China's most important virology institutes. Within a short time, numerous illnesses and deaths of people due to acute respiratory failure occurred in the city. An aetiological agent, a previously unknown coronavirus, was quickly identified and named SARS-CoV-2. Despite difficult experiences with the pathogenic coronaviruses SARS, identified in 2003, and MERS, detected in 2012, it seemed to be only a local infection, and not much was done to prevent the disease from spreading outside China. However, by quickly spreading globally, COVID-19 conformed to the definition of a pandemic.

The World Health Organization (WHO), as a specialised agency of the United Nations dealing with the protection of health worldwide and committed to work with countries and partners to unite the world to jointly face a common threat, has come to occupy a special place in the global fight against COVID-19. Six regional offices and 150 national offices are working closely with governments around the world to make

their health systems respond more effectively and compatibly to COVID-19. The WHO has set up the COVID-19 Solidarity Response Fund to provide frontline staff with the necessary materials and information and accelerate research into vaccine and drug development. A web portal with current news about COVID-19 was launched and information materials on the pandemic were prepared specifically for the countries of the developing world, providing accurate information and debunking dangerous myths [36]. This includes hundreds of technical tips for the public, health professionals, including evidence-based guidance for each element of the plan for reacting to COVID-19 [37]. In doing so, the health agency draws on the expertise of a global network of health professionals and researchers, including epidemiologists, clinicians and virologists, to ensure that the knowledge it disseminates is authoritative and representative. Many social media and technology companies work closely with the WHO to assist in the flow of reliable information. The WHO has sent more than two million items of personal protective equipment (PPE) to 133 countries, and at the time of writing (December 2021) is preparing to send another two million items. Additionally, more than a million diagnostic tests have been sent to 126 countries in all regions, and more are being acquired. The WHO is working with the International Chamber of Commerce, the World Economic Forum, and other private sector organizations to increase the production and distribution of essential medical supplies. It has also set up a 'task force on the UN COVID-19 supply chain', which aims to dramatically increase deliveries of essential protective equipment where it is needed.

The organisation also intends to train millions of health workers through its Open WHO platform. With this on-line tool, lifesaving knowledge is shared with first responders by the organisation and its key partners. Countries are also supported by experts distributed worldwide in the WHO Global Outbreak Alert and Reaction Network (GOARN). The WHO has also launched the international clinical 'Solidarity Trial' of drugs against coronaviruses involving 90 countries. It has developed research protocols used in more than 40 countries, and continues to play a key role in the ongoing pandemic. Criticism of the WHO's slow action at the start of COVID-19 is already leading to a restructuring of the organisation to make it more capable of responding effectively to future global health crises.

The European community has also undertaken to coordinate the action of its 27 member states. This includes improving the supply of medicines and medical equipment, standardising treatment, securing cross-border transport and the flow of goods, treating patients from neighbouring countries, developing financial tools to support workers and healthcare industries, and pooling resources to find and optimise the procurement and distribution of an effective COVID-19 vaccine or anti-virus medicines. The European Centre for Disease Prevention and Control (ECDC) in Stockholm, Sweden, has been strengthened with more staff and funding. Action significantly broadening the area of competence in epidemiology and raising the importance of the ECDC improves its capacity to advise member states. Similarly, EU networks for exchanging information about hazards such as the Early Warning Response System (EWRS) have been fortified. Such coordination is essential to strengthen the capacity of the EU to act on behalf of all member States in the healthcare sphere.

An important direction is the development of methods for the surveillance and tracking of contacts, including interoperable applications for smartphone, that require minimal data, are voluntary, and comply with privacy laws and the highest standards of information security. Some of them were implemented by individual countries, an example of which is the EU Digital Covid Certificate.

Attention should fall particularly on research and development, which are the main pillars of the European strategy to strengthen innovation and competitiveness on the continent. The continent's research capacity should be supported in such a way that decision-makers can quickly make informed decisions in crisis situation. A way to make this possible would be to turn the European Research Area (ERA) into a dynamic and targeted catalyst for innovation in the fight against pandemics.

The COVID-19 pandemic and NATO. *'With the outbreak of COVID-19 pandemic, for the first time in its history NATO had to face an attack against each of its member states at once.'* These are the opening words of an extensive article by an eminent analyst, Dr. Giovanna de Maio of the University of Washington [38], which was published in December 2020 on the pages of *Foreign Policy*, one of the most important political science journals in the world. The quote shows the gravity of the situation and actually puts beyond discussion how serious it is. It might be added, however, that the pandemic has created a unique opportunity to hone the mass response of alliance to a whole new threat. NATO has taken advantage of this opportunity by supporting civilian efforts and providing military air transport, establishing field hospitals, and sharing its experience of military medicine. The Euro-Atlantic Disaster Response Coordination Centre (EADRCC) is NATO's main crisis response mechanism. The centre operates 24 hours a day, 7 days a week, coordinating requests and support offers. It also helps coordinate assistance, including medical and financial support. A NATO Pandemic Response Trust Fund has been set up to enable rapid procurement of medical supplies and services. The NATO Pandemic Response Trust Fund maintains stocks of medical equipment and supplies in order to be able to provide immediate assistance to allies or partners in need. Logistical support provided by the NATO Support and Procurement Agency (NSPA) has helped allies and partners purchase supplies to help fight COVID-19. The agency manages the purchase and storage of aid items at the NSPA's Southern Operational Centre in Taranto, Italy. NATO works closely with other international organisations, including the European Union, CDC and National Institutes of Health (NIH) in the USA, the ECDC, and the UN (mainly the WHO, a UNICEF–World Bank partnership, and the Food and Agriculture Organization (FAO)). Since the beginning of the crisis, the EADRCC has been considering requests for assistance from the UN and partner countries. More than 130 applications were acceded to. The delivery of aid to NATO partners, such as Bosnia and Herzegovina, the Republic of Moldova, North Macedonia, Georgia, Ukraine and others, is coordinated.

In the first half of 2020, nearly half a million NATO troops supported civilian efforts in building field hospitals, offering assistance in research, transporting patients, distributing medical equipment, evacuations, helping with decontamination, providing laboratories and quarantine

sites, and organising segregation centres. The military forces of NATO members have carried out more than 350 flights to transport medical personnel, transported more than 1,000 tons of equipment, and helped build nearly 100 field hospitals and provide 25,000 treatment beds.

NATO supports innovation through research and scientific collaboration on COVID-19. The NATO Science & Technology Organization (STO) supports research and scientific collaboration on COVID-19, e.g. in pandemic modelling or in optimising rapid diagnosis of the disease. The STO maintains contact with 6,000 scientists, including some from Poland. More than 40 projects are being carried out, e.g. countering pandemic disinformation ('fake news' and anti-vaccination movements), or the optimisation of relief operations in pandemic situations.

The lessons learned, or what has the COVID-19 pandemic taught us? The scientific and technological progress in the field of antibiotic therapy, vaccinology and methods of prevention and treatment of infectious diseases that has taken place over the past 100 years is without any precedent in previous ages, and allows us to look calmly to the future. However, the COVID-19 pandemic has shattered the illusion of the naive that the dangers of infectious diseases are a thing of the past. International organisations and governments world must once again take into account the unpredictable risk factor of infectious diseases, both in the context of natural epidemics and biological warfare. The man/animal-microorganism-environment triad undergoes constant natural evolution. New emerging infectious diseases begin to threaten man, and old but no less dangerous ones return (diphtheria), which sometimes have evolved and become drug-resistant (e.g. the extensively drug resistant strains of tuberculosis or drug-resistant plague in Madagascar) – the re-emerging infectious diseases. The neglected diseases, such as malaria, amoebiasis, leishmaniasis, etc., still claim millions of victims. Before our eyes, the species barrier of a number of zoonoses is being crossed, which is a spill-over phenomenon and is best exemplified by the coronaviruses (SARS, MERS) [39].

Biosecurity [17, 40] when taken to mean the restrictions on the possession, processing and transfer of biological dual-use agents, is an important element defining non-proliferation policy [41, 42]. However, this zone of activity is not managed on the global scale in a way which inspires confidence. To date, only partial control of international transfers of dual-use items has been achieved on the basis of a voluntary agreement by the signatories of the Australia Group [13]. Unfortunately, however, it has not been possible to achieve binding international agreements (despite the establishment of the international Ad Hoc Group for Medical Research in 1994), because the relevant regulations adopted in the EU [43], the US and other countries of the developed world, are not respected by all other countries.

In this context, there is concern about the unresolved dispute about the origin of the SARS-CoV-2 virus, as a natural phenomenon or as the artificial result of genetic manipulation. Has the next coronavirus (after SARS and MERS) crossed the species barrier from bats to humans, or is it a hybrid produced in the laboratory [44]? If it was created in a laboratory, is it a hybrid derived by chance solely for research purposes (gain of function), or intentionally for military purposes? These questions and the lack of a transparent investigation in China

were some of the reasons for the emergence of suspicions about the unnatural origin of this virus [45, 46]. Indeed, at the Wuhan Institute of Virology, research was underway to study the potential pathogenicity of coronaviruses and to change the host [47]. Of particular concern is the appearance of a furin cleavage site in the S protein and the presence of an atypical arginine codon, which determine the pathogenicity of the virus. Current methods of site-specific mutagenesis are generally very difficult to detect when used, but this codon may provide a clue indicating an intentional effect. It is suspected that the change in host specificity could also have occurred accidentally after isolation of coronaviruses from bats, and during experiments passaging the virus through different cell lines [48] or humanised mice [49]. The epidemiological and virological arguments pointing to an artificial origin of the virus appear to carry equal weight to or even outweigh those pointing to its natural origin [50].

In summary, State regulations covering the licensing and supervision of research or diagnostic work would both limit the undertaking of these types of risky experiments and provide evidence for investigation when called for. It is worth noting that many member States of the UN and signatories of the Biological and Toxin Weapons Convention, including Poland, have not yet implemented the relevant provisions arising, for example, from the UN Security Council resolution of 2005 (UNSCR 1540). As opposed to chemical or nuclear agents, biological agents more often than not are not included in the purview of binding legal mechanisms of a national or international nature. This is an important gap in the law which was noticed by specialists after the anthrax attacks in 2001, and which the international community must revisit. Since 2001, many countries have rectified this omission, but many have not done so.

The COVID-19 pandemic highlighted the shortcomings in the global monitoring of biological threats, especially from the aspect of the tardy and uncoordinated response of countries to the outbreak in Wuhan, including the WHO, and political procrastination imputed to its authorities. However, it should be remembered that as far back as 2002, the authorities of the Peoples' Republic of China delayed notifying the UN about the outbreak of the SARS epidemic. They were obliged to make the notification as a member of the UN by the WHO's *International Health Regulations (IHR)* [51]. A similar reprehensible delay involved the concealment in 2013 by West African countries of the extensive Ebola outbreak. The contribution which could be made by rapid exchange of information on biological hazards is therefore growing [52]. For years, this situation has been continuously monitored globally under the IHR, an activity termed 'epidemiological surveillance', a rational supervision based on the fifth edition of the IHR of 2005. A total of 194 WHO member States have since completely amended these provisions. There was a shift from nosological criteria (evaluating disease by quarantinable status) to syndromic criteria (evaluating on a set of suspicious symptoms), combined with an assessment of the epidemiological situation in the country of the patient afforded by the *surveillance*. However, this requires upgrading the status of the IHR, to legally enforce and repair the politically-engendered weakness it has. At least three times in recent years, political correctness has delayed the detection of the most dangerous epidemics, allowing them to spread catastrophically. The global alarm caused by the emergence of COVID-19 triggered restrictions too late on

international traffic and border restrictions, despite the noble intentions in the maxim ‘Global alert – global response’, which had been the theme of World Health Day in 1997. Support is crucial for international NGOs, whose activities have already proved invaluable on several occasions (e.g. those of Médecins Sans Frontières).

Creating a system for the protection of public health is necessary and achievable in any country, regardless of the political system and degree of economic development, and when carried out simultaneously it strengthens global healthcare. This is the readying of the related critical elements not only of the public services of the State, but also the preparation of citizens through education, training, immunisation, and equipping them with PPE. Providing this equipment can pose a significant challenge to the provisioning infrastructure of the healthcare system and emergency and law enforcement services, as well as the whole of the society involved. The size of the challenge depends on the route of transmission of the epidemic’s aetiological agent and on the agent itself. The scale of needs varies depending on the specific population exposed. During the bioterrorism attacks, PPE was mainly used by the emergency services, while during the subsequent flu pandemics and wider need, it was difficult to provide adequate amounts of PPEs. However, it was only during the COVID-19 pandemic that the disruption of supply chains and the disparity between supply and demand showed how important it is to have domestic production site, and not rely only on imports. Important elements that offset the shortfalls in this area were government reserve agencies and the mutual assistance of other countries.

Three elements of the system for protection against particularly dangerous diseases may be enumerated as those necessary for the effective defence State [53]: the first two are diagnosis in high-level biosafety laboratories and means of safe transport of patients in conditions that allow maintenance of their vital functions (e.g. Trexler-type isolators). The third is High-Level Isolation wards, otherwise known as High Security Infectious Disease Units (HSIDs), allowing safe isolation of the patient, while ensuring that neither intensive care nor safety of personnel are compromised by facilitating work under negative pressure with HEPA filtration. In particular, this last element has been and still is a matter of concern. The health care system operates in a state of chronic shortage of funds and an increasingly scarce supply of medical personnel, which meant that during the pandemic, a few infectious disease units were unable to admit all needed COVID-19 patients in their catchment area. In many hospitals, the operation of regular wards was suspended and in the place of those wards temporary infectious disease wards or a temporary hospital were created. This had adverse consequences both for uninfected patients who were unable to receive the care to which they were entitled, and for the level of care provided to COVID-19 patients, which was sometimes late and rarely provided by infectious disease specialists, of whom there were suddenly too few. Although corrective action had already been taken following the anthrax attacks and later influenza pandemics, it was not until the occurrence of the COVID-19 pandemic that the readiness of the health system to meet such challenges was tested and found wanting. These lessons have not been learned. Therefore, there are still demands to expand the personnel resources in infectious disease specialisations, to prioritise this field of medicine, to increase the number

of infectious disease wards, and to prepare in advance the infrastructure and equipment of temporary hospitals based on selected units of the system.

The threat of a pandemic of SARS and seasonal influenza called for action to effectively prevent infections that spread through the respiratory tract, and led the WHO and the CDC in Atlanta, USA, to implement non-pharmaceutical interventions/measures, in the official WHO/CDC terminologies. Proving themselves prescient, the measures were appropriate for the COVID-19 pandemic and fell into two divisions: steps taken individually and measures imposed on society as a whole. These are both actions (disinfection and wearing FFP3 masks) and refraining from actions (e.g. avoiding social contacts and observing lockdown in large urban centres of population). A pioneering comparative review of non-pharmaceutical measures in Poland and a number of countries worldwide was discussed in the comprehensive study by Anna Świątecka [54]. Lockdown is a very effective, but economically and socially drastic means of combating epidemics (especially those that spread through the respiratory tract) by reducing human contact. It requires the readiness and consent of societies to bear the costs of the consequent reduction in economic activity, and to endure everyday life becoming far more difficult. How much is required of societies is evidenced by the current social unrest, the rise of conspiracy theories, and anti-vaccination movements in a number of developed countries around the world.

Diagnosis – especially rapid diagnosis – is a very important part of the fight against any epidemic [55]. Maintaining the capacity and resources to diagnose individual biological agents is an important undertaking by the State in the domain of biosafety. In addition to the known risk elements referred to previously (the ‘Dirty Dozen’ and list extensions), infectious diseases and completely hypothetical and hitherto unknown biological agents are emerging. Maintenance of a state of readiness to act swiftly and find diagnoses seems to be an indispensable element of the effectiveness of the system for the biological hazard preparedness of any State. Nevertheless, a multiplicity of factors, often exotic or rare, and a lack of developed and validated diagnostic systems, limit the effectiveness of such preparations. This makes it necessary to increase the inventory in diagnostic laboratories, or to have parts of it in rotating allocation. Preparedness in the narrow diagnostic sense is helped by a new and increasingly available technique for precise hazard typing – the rapid next-generation sequencing of isolates. This allows the rapid diagnosis of new threats and has proved its usefulness, both against the influenza virus and during the COVID-19 pandemic. Determination of the genetic sequence of new isolates not only allows their origin to be deduced, but also makes it possible to establish diagnostic markers, pathways of spread, and the potential pathogenic risk. Modern DNA synthesis technology, combined with the rapid distribution of genetic diagnostic marker data, allows the reproduction of PCR-based detection methods at multiple sites without access to the isolate. However, the use of this technology, and other classical ones for rare or emerging agents, requires the maintenance of trained personnel and equipment, which was proved both during the anthrax attacks, influenza outbreaks and the COVID-19 pandemic, when Reference Laboratories were the first to respond. In Poland, these were the laboratories of the National Institute of Public Health

and National Institute of Hygiene (NIZP-PZH), the National Veterinary Institute (PIWet) and the Biological Threats Identification and Countermeasure Centre of the Military Institute of Hygiene and Epidemiology (ODiZZB WIHE).

The experience from the time of the bioterrorist attacks has justified keeping these authoritative units appropriately supplied with reagents and qualified personnel, and engaging their scientists not only in routine clinical diagnostics but also in research work. The latter is the right direction for the activities of these laboratories because it preserves their flexibility and facilitates rapid implementation of new methods and new directions of diagnostics. However, a still noticeable flaw in the guaranteed provision of national diagnostics capacity is the lack of a laboratory at biosafety level 4 (BSL-4, containment level 4) [56], which may be required for the response to future threats. In a crisis situation, the problem of access to such a laboratory and the impossibility of fast and safe transport to EU reference centres may delay a diagnosis which is critical to further investigation.

Imperfect risk monitoring and underestimation of risks, the weakness of epidemiological surveillance services, the ineffectiveness of medical intelligence gathering, and no more than passive observation of the countries affected by the outbreak were the reasons for the initial uncontrolled expansion of the pandemic. Going forwards, it is necessary to strengthen national and EU response systems, endowing them with better monitoring and early detection of threats, and it is also necessary to take rapid decisions to prevent the spread of diseases.

The COVID-19 pandemic has also brought greater than previously encountered (although not always effective) improvements in solidarity and international cooperation as an embodiment of the 'One Health' approach. This has led to an unprecedented collaboration between theoretical and applied science to produce effective vaccines based on new technologies (mRNA) in record time. The prevailing pandemic has deepened our understanding of the dynamics of epidemic processes, and seems to verify the statement made at the World Bank forum: 'there are no incurable diseases – there are only under-invested ones.'

SUMMARY

The unexpected emergence and rapid pandemic development of the new COVID-19 disease, caused by the hitherto unknown SARS-CoV-2 coronavirus, has demonstrated the threat of infectious diseases to the whole world. The dispute over the origin of the virus has re-ignited discussions on all aspects of the non-proliferation policies and biological weapons. In taking millions of lives and wreaking havoc in many branches of human activity, COVID-19 is encouraging some undemocratic countries and terrorist organisations to use biological agents on a large scale. Bioterrorist attacks are now more likely to be carried out, in particular given the progress in the modification of biological agents and the revolution in the means of their delivery. The line is blurring between the deliberate production of biological weapons or material for bioterrorism and dangerous scientific grant-supported research with the professed purpose of serving the good of humanity. In turn, however, the COVID-19 pandemic has led to a great mobilisation of science and industry, and through this to the production of effective

vaccines in a shorter time than history has ever known. This mobilisation has also achieved vaccine production based on the pioneering technology of mRNA. The pandemic has brought speedy gain, political uniformity (reducing the striking health inequalities, of which one manifestation is the differences in access to vaccines worldwide) and sufficient economic support for global systems for the detection, prevention and counteraction of pandemic biological threats, irrespective of their origin. Among the most important responsibilities which this and bioterrorism leave us with, are the improvement in international control over the flow of materials and technologies, supervision of the biotechnology industry, modernisation of early warning systems, and ensuring worldwide access to rapid diagnostics, supplies of vaccines, medicines, equipment (respirators, isolation boxes, oxygen generators, etc.), and non-pharmaceutical measures. Training and exercise opportunities should be provided, and response plans developed and updated to take into account mass isolation and quarantine. Modern contact tracing systems are to be developed and implemented. The establishment of a uniform international diagnostic and hospital structure should be pursued, guaranteeing the provision of medical assistance at scale, and thus the elimination of the selfishness of rich countries towards the poor and under-developed. A global solidarity fund should be set up to combat biological threats. Global coordination in the areas of action, technology transfer and modern knowledge will be necessary, for which the key will be the founding of facilities capable of rapidly shifting from production to fighting a pandemic, and fulfilling needs for vaccines, diagnostic kits, respirators, protective equipment, masks, and disinfectant preparations. Worldwide spending on the science needed to combat future biological threats should be increased. The global shock caused by the pandemic has shattered humanity's false sense of safety from infectious diseases. It has also exposed hitherto unknown problems and areas neglected in the proliferation naturally to be expected in a globalising world, and shown the need to control and combat bioterrorist threats.

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