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Pandemics, epidemics, bioterrorism: challenges against public order

Introduction

Covid-19 is a highly contagious, coronavirus-caused disease of zoonotic origin, characterised mainly by respiratory and general febrile symptoms, which represents mainly public health risks, while its veterinary significance is minimal¹, though some animal species are susceptible which may represent ecological risks².

The first reports arrived from Wuhan city in the Hupei region of China, the first officially admitted positive sample was taken 8th December 2019. ³ The virus spread to several countries of East-Asia, and later it also appeared in Europe. The first officially recognized positive sample was collected in Italy 23rd January 2020. The World Health Organisation declared the infection as pandemics in March 2020, and in April 2020 already 210 countries and geographical entities reported the presence of the infection.

Covid-19 is the abbreviation of the full name of the disease (<u>co</u>rona <u>vi</u>ral <u>disease</u> - 20<u>19</u>), and is caused by the SARS-CoV-2 virus (<u>Severe A</u>cute <u>R</u>espiratory <u>S</u>yndrome <u>Co</u>rona<u>v</u>irus type <u>2</u>). A close relative of this virus appeared in the beginning of this century in 2002, and was designated as

Source: https://journals.asm.org/doi/epub/10.1128/JVI.00083-21

¹ Tiwari, R., Dhama, K., Sharun, K., Yatoo M. I, Malik, Y. S., Singh, R. (2020): COVID-19: animals, veterinary and zoonotic links, Veterinary Quarterly 40, 169-182

² Palmer, M. V. et al (2021): Susceptibility of White-Tailed Deer (Odocoileus virginianus) to SARS-CoV-2, Journal of Virology, 95.

Sharun, K. et al. (2021): SARS-CoV-2 in animals: potential for unknown reservoir hosts and public health implications, Veterinary Quarterly 41, 181-201

³She, J., et al. (2020): 2019 novel coronavirus of pneumonia in Wuhan, China: emerging attack and management strategies. J. Transl. Med. 9 (1), 19–19. doi: 10.1186/s40169-020-00271-z

the SARS virus, but since the appearance of the new type it has been renamed as SARS-CoV-1. This virus caused an epidemic between November 2002 and June 2003, and, although 8096 proven infections were reported from 16 countries of the Earth, the infection disappeared, partly due to the introduced control measures. It must be mentioned that 774 patients died from the infection (9.56%), which means a much higher mortality rate then we experienced in the present Covid-19 epidemics (1.3%).⁴

SARS-CoV-1, SARS-CoV-2 and their closest relative of animal origin RaTG13, demonstrated in horseshoe bats, although they are very close phylogenically, are significantly distinct genetically. The difference in the nucleic acid genome is about 4% (this genomic difference in the case of humans and chimpanzees is about 1%), which suggests the mediatory role of a so far unidentified animal species in the transmitting of the virus from bats to humans. SARS-CoV-2 seems to be a virus highly adapted to humans, and not a virus which shifted its host recently. The cause of the changes resulting in the enhanced capacity in infecting humans was investigated, and the role of an otherwise not too difficult artificial genetic modification arouse, because these evolutionary gaps have generated debates from the beginning regarding the laboratory origin of SARS-CoV-2. Though no solid evidences support these theories, they were enhanced when it turned out that in the Wuhan Institute of Virology (WIV) experiments financed by the American National Institute of Health (NIH) were carried out to adapt bat viruses to human cells to produce vectors used in gene therapy (https://www.niaid.nih.gov/diseases-conditions/coronavirusbat-research). Despite these speculations, presently the dominant opinion of the virologists and epidemiologists is that the SARS-CoV-2 is not a laboratory escapee, even though the animal species transmitting the virus from bats to humans has not been possible to identify so far.⁵

Source: https://doi.org/10.3389/fcimb.2021.596201

⁴ Kumar, A. et al. (2021): Wuhan to World: The COVID-19 Pandemic, Frontiers in Cellular and Infection Microbiology, 11.

⁵ Holmes, E. et al. (2021): The origins of SARS-CoV-2: A critical review, Cell 184, 19, 4848-4856

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Epidemiology

Though the virus is of animal origin, now it spreads among humans mainly by aerial route (droplet infection) and eventually by contact contamination. The surgical masks or even homemade textile masks have effectively inhibited the spread of the virus by preventing the droplet infection, while the frequent washing of hands, the disinfection of surfaces (handles, doorknobs, handrails etc.), avoiding the traditional greetings (handshakes, kisses etc.) have reduced the possibility of contact contamination. Still, the most important factor to slow down the spreading of the epidemic was the reduction of social contacts: closing the schools, the introduction of online education, encouraging home office working, imposing visit bans in certain institutions (hospitals, nurseries etc.). The countries introducing these measures fast and effectively to alleviate the pressure on the healthcare system by flattening the epidemic curve mostly could avoid the rapid increase of case numbers and mass infections. The role of the law enforcement organizations in the maintenance of the epidemic controlling measures (border control, enforcement of curfew restrictions, supervising home quarantined patients and mask wearing in public places etc.) is summarized elsewhere.⁶

The genome of the SARS-CoV-2 coronavirus mutates rapidly, and several variants of the virus have emerged in the past two and a half years. After the original "Wuhan" strain soon emerged the British (Alpha), the South-African (Beta), the Brazilian (Gamma) and another South-African (Omicron) mutant, which led to new epidemic waves worldwide,⁷ including Hungary.

⁶ Gömbös, S. (2022): Rendőrség a koronavírus-járvány elleni küzdelem szolgálatában.[Police in the fight against the coronavirus epidemic] Rendőrségi Tanulmányok, 2022/2

⁷ Schwarzendahl, F. et al. (2022): Mutation induced infection waves in diseases like COVID-19, Scientific Reports 12.

Source: https://doi.org/10.1038/s41598-022-13137-w

Each new variant had a higher infectivity, but reduced virulence compared to the previous ones. This fact was reflected in the epidemiological data, since the number of people infected per day peaked always higher, but the number of hospitalized people did not run at the same time. It was highest in the 3rd wave caused by the Alpha variant, it was significantly lower during the 4th (Delta) and even lower in the 5th (Omicron) epidemic wave. The same phenomenon can be observed in the number of Covid-19 casualties and in the number of people needing intensive care (life support machine treatment): both were the highest in the case of the 3rd (Alpha) wave.

Pathogenesis, symptoms

The early variants (Wuhan, Alpha) of the virus caused occasionally unapparent infections or mild respiratory symptoms, but the consequence was a severe illness in most cases. It is well-known that the severity of the Covid-19 is age-dependent, and the most severe symptoms are expected in elderly people, though there are exceptions to this rule. Age is a risk factor, since with growing age the chronic health problems like diabetes, hypertension, cardiovascular diseases (coronary stenosis, previous heart attack, chronic heart failure etc.) are more frequent. Covid-19 may lead to the misbalance of treated hypertension, keeping this vital biological parameter among physiological values. This may lead to a life threatening condition which may even be fatal, since the virus multiplication causing focal heart muscle cell necrosis also contributes to the reduction of cardiac output and the collapse of the blood circulation. Overweight is also a risk factor, since it also represents an extra burden to the circulatory system. Moreover, the most important risk factors (obesity, hypertension, diabetes) very frequently appear simultaneously.8

⁸ Zhang, J.et al. (2020): Risk factors for disease severity, unimprovement, and mortality in COVID-19 patients in Wuhan, China, Clinical Microbiology and Infection, 26, Issue 6, 767-772

Patients usually have high fever accompanied by the usual, general, febrile symptoms: apathy, inappetence, nausea, muscle pains, fatigue etc.). Acute pneumonia is developed, and after 8-10 days the inflammatory process may turn into an escalating immunological overreaction called "cytokine storm", which may be fatal. In these cases, it is not the viral damage of the organs that will cause the problems, but the too strong (allergic) immunoreaction may lead to the paralysis of the vegetative functions.⁹ If the cytokine storm is avoided and the patient survives the acute pneumonia, the replacement of the pneumocytes will start, connective tissue cells will proliferate and lung fibrosis may be the consequence.

Symptoms	Occurrence
Fever	83–99%
Cough	59-82%
Inappetence	40-84%
Fatigue	44-70%
Dyspnoea	31-40%
Bronchial exudate	28-33%
Muscle pain	11-35%
Ageusia/anosmia	10-30%
Skin rash	10–15%

The most frequent symptoms of Covid-19 are listed in the table below:

The lung oedema and the exudate accumulating in the lower parts of the respiratory system due to pneumonia will lead to puerile breathing and causes clearly recognizable alterations in X-ray and CT examinations.

The infection frequently causes loss of sense of taste and smelling (ageusia and anosmia), presumably because of the degeneration of the supporting

⁹ Ye, Q., Wang, B., MaoJ, .H. (2021): The pathogenesis and treatment of the `Cytokine Storm' in COVID-19, Journal of Infection, 80, 607-613. Source: https://doi.org/10.1016/j.jinf.2020.03.037

cells around the olfactory and taste receptors, which causes a usually transitional functional disturbance in these sensors. (The neurons and the receptors themselves usually do not degenerate; hence the functional changes in the smelling and tasting ability are only transitional.) The occasionally observed diarrhoea is the consequence of the intestinal epithelial degeneration caused by the virus inducing enteritis.

The lung is usually not damaged in the infections caused by the recently emerging mutants (most of all the different strains of the Omicron variant), mostly symptoms of the inflammation of the upper respiratory tract are characteristic (sore throat, asperity of the voice, coughing, nasal discharge etc.). Besides these, general symptoms (fever, inappetence, headache, fatigue, depression) are also frequent, as well as the ageusia and anosmia. Since pneumonia does not develop, in the infections caused by the Omicron variant the cytokine storm seldom evolves. That is why the number of patients needing intensive care or dying because of health problems due to Covid-19 has been much lower since the Omicron variant became dominant.¹⁰ Evidence suggests it is less severe than previous variants,¹¹ especially compared to Delta.¹² BA.1 might be less able to penetrate deep lung tissue. Omicron infections are 91 percent less fatal than the delta variant, with 51 percent less risk of hospitalization.¹³

Source: https://doi.org/10.1128/jvi.00961-22

¹⁰ Fan, Y. et al. (2022): SARS-CoV-2 Omicron variant: recent progress and future perspectives, Signal Transduction and Targeted Therapy 7.

Source: https://doi.org/10.1038/s41392-022-00997-x

¹¹ Bálint, G., Vörös-Horváth, B., Széchenyi, A. (2022): Omicron: increased transmissibility and decreased pathogenicity, Signal Transduction and Targeted Therapy 7:151. Source: https://doi.org/10.1038/s41392-022-01009-8

¹² Nyberg, T. et al. (2022): Comparative analysis of the risks of hospitalisation and death associated with SARS-CoV-2 omicron (B.1.1.529) and delta (B.1.617.2) variants in England: a cohort study. Lancet. 2022 Apr 2;399(10332):1303-1312. doi: 10.1016/S0140-6736(22)00462-7. Epub 2022 Mar 16.

Martins, M. et al. (2022): The Omicron Variant BA.1.1 Presents a Lower Pathogenicity than B.1 D614G and Delta Variants in a Feline Model of SARS-CoV-2 Infection. Journal of Virology, 96:17.

¹³ Lewnard, J. A. et al. (2022): Clinical outcomes among patients infected with Omicron (B.1.1.529) SARS-CoV-2 variant in southern California. Nature Medicine.

If symptoms emerge or re-emerge 4-6 weeks after the onset of the disease, it is called long-Covid or post-Covid syndrome. The most frequent symptoms are fatigue, dyspnoea, chest pains, lack of concentration, insomnia or nightmares. The syndrome may last for several weeks.

Symptom	Occurrence
Fatigue	(58%)
Headache	(44%)
Loss of hair	(25%)
Dyspnoea	(24%)
Ageusia/anosmia	(23%)
Joint pains	(19%)
Mental disorders	(16%)

The most frequent post-Covid symptoms:¹⁴

In children even inapparent infection may lead to multisystem inflammatory syndrome (MIS-C), when severe inflammation of one or more vital organs is observed, indicted by high fever and caused by panarteritis.

Diagnostics

As in the case of most virus infections, for the demonstration of SARS-CoV-2 the polymerase chain reaction following reverse transcription (RT-PCR) 2 is considered the most sensitive method internationally. While PCR demonstrates the presence of the viral genome in the samples, the rapid antigen-detection tests are also wildly used, and demonstrate the protein

doi: 10.1038/s41591-022-01887-z.

¹⁴ Han, Q., Zheng, B., Daines, L., Sheikh, A. (2022): Long-Term sequelae of COVID-19: A systematic review and meta-analysis of one-year follow-up studies on post-COVID symptoms, Pathogens, 11(2), 269;

Source: https://doi.org/10.3390/pathogens11020269

components of the virus. Viruses are obligatory cell parasites, they penetrate into the cells, and force them to produce their genome and proteins. This process causes cell damage, and the cells usually die and are lysed at the end of the virus production. The different body fluids and products (i.e. nasal discharge, saliva) contain the viral genome and viral proteins (antigens) in high amount in certain periods of the disease, when a lot of cells are damaged. The rapid antigen-detection tests are able to detect the antigen if it is present in high concentration, but the PCR is able to detect even a few genomes. That is why the golden standard method of the SARS-CoV-2 coronavirus diagnosis is the PCR. The virus can be detected a few days earlier in the body fluids by the use of this method, and the genome can be detected days or sometimes weeks after the antigen demonstrating tests turn negative. Altogether, in the case of an infection, the PCR turns positive sooner, and remains positive longer then the antigen demonstrating tests. PCR is also suitable for the identification of the types and subtypes of the SARS-CoV-2 causing the infection.¹⁵

The virus multiplying in the intestinal epithelium will be excreted with the faeces, while the virus multiplying in the kidney will appear in the urine, but these body products play minor role in the transmission of the disease, that is why mainly the respiratory excretions are used for diagnostic purposes. At the same time, due to the presence of the virus in the stool and urine, the sewage indicates the amount of the virus circulating in the population well. If there are many infected people in a city (region), then in the samples taken at the regional sewage plant the concentration of the coronavirus genome will be high. This is a very important predictive indicator, since if the concentration increases or decreases in the second of two samples taken at different times, then presumably the number of the infected people will rise or drop respectively in that region in the next few days.¹⁶

Source: https://doi.org/10.1002/mco2.115 ¹⁶ Shah, S.et al. (2022): Wastewater surveillance to infer COVII

¹⁵ Aliabadi, H. A. M. et al. (2022): COVID-19: A systematic review and update on prevention, diagnosis, and treatment, MedComm Wiley Online Library.

¹⁶ Shah, S.et al. (2022): Wastewater surveillance to infer COVID-19 transmission: A systematic review. Science of The Total Environment 804.

The infection activates an immune response, antibodies are produced, and the virus will disappear from the body after two or three weeks, or at least it cannot be detected by direct methods from the nasal and pharyngeal samples. The indirect methods proving the survived infection are based on the detection of SARS-CoV-2 specific antibodies. Most of these tests are based on enzyme reactions and will indicate the presence of antibodies in the blood or serum with colour reaction. The fast tests working with full blood samples (i.e. rapid test kits working with one or two droplets of fingertip blood) are usually less sensitive and specific. The laboratory ELISA (Enzyme Linked Immuno-Sorbent Assay) tests are suitable for serological investigations, and are more exact and reliable.¹⁷

Treatment

In the early phase of the pandemics, drugs developed and used previously for the treatment of other infections ("repurposed medicines") were applied to hinder the multiplication of the virus in the human body, and mitigate the symptoms of Covid-19. These were the Favipiravir developed against influenza and the Remdesivir used in the treatment of Ebola fever. Many pharmaceuticals were tested, but proved to be inefficient, such as chloroquine and hydroxychloroquine used in the treatment and prophylaxis of malaria, and the antiparasitic ivermectin. The efficacy of these drugs was not unambiguously proven in clinical trials. In the later phase of the pandemics, specific chemotherapeutic agents against SARS-CoV-2 (polymer-ase and protease inhibitors) were designed; the best known and wildly used among these are molnupiravir and Paxlovid.¹⁸

Source: https://doi.org/10.1016/j.scitotenv.2021.150060

¹⁷ Aliabadi, H. A. M. et al. Ibid.

¹⁸ Cantini F., Goletti D., Petrone L., Najafi Fard S., Niccoli L., Foti R. (2020): Immune therapy, or antiviral therapy, or both for COVID-19: a systematic review. Drugs 80, 1929–1946.

Source: https://doi.org/10.1007/s40265-020-01421-w

Besides chemotherapy, different immunotherapeutic treatments were also used, mostly monoclonal antibodies, usually as mixtures ("cocktails"), distributed under different names (Bamlanivimab, Sotrovimab, Casirivimab, Imdevimab etc.), but all common in their mode of action: they adhere to the spike protein of the SARS-CoV-2 and block the adherence of the virus to the cell receptor, hence reduce the chance of infection and the number of the infected cells. The use of the sera of reconvalescent people in the therapy (plasma therapy) was based on the same theoretical background.¹⁹

All these therapeutic products are able to reduce the virus multiplication and alleviate the symptoms, giving time and chance to the immune system of the treated patient to overcome the infection. During the cytokine storm and the breathing difficulties oxygen inhalators or, in the most severe cases, intubation in anaesthesia, furthermore anti-inflammatory treatment were employed to prevent the harmful effects of the immunological overreaction.²⁰

Prevention

Presently 13 vaccines of different types are approved for the prevention of Covid-19 in Hungary.²¹ They contain either the inactivated SARS-CoV-2 virus, or the nucleic acid carrying the genetic information of the spike protein. Inoculation of these vaccines aims to increase the resistance of the organism by inducing immunity artificially. Antibodies generated in the higher organism following the vaccination will react with the spike protein and prevent the attachment of the virus to the surface of the cells, block its penetration and the consequent virus multiplication. Following vaccination

¹⁹ Ibid.

²⁰ Wen, W. et al. (2022): Efficacy and safety of three new oral antiviral treatment (molnupiravir, fluvoxamine and Paxlovid) for COVID-19: a meta-analysis. Annals of Medicine 54, 516-523, Source: https://doi.org/10.1080/07853890.2022.2034936

²¹ Source: https://covid19.trackvaccines.org/country/hungary/

a certain level of immunity will develop against the pathogenic microorganism, and if enough people are immunized, population-level immunity, commonly called "herd immunity" will be reached within the given society. Besides being less susceptible to the infection, immunized people produce less severe symptoms even if infected, and much fewer viruses are produced and shed by them, hence their role in the spreading of the disease is not significant.

The six vaccines from among the 13 approved ones used from the second year of the pandemics in Hungary were the following:

- 1. BBIBP-CorV (produced by Sinopharm) is a traditional, first-generation vaccine containing formalin inactivated complete virus, adjuvated with aluminium salts to increase its immunogenicity, and completed with preservatives to elongate its tenability.
- 2. Comirnaty (produced by Pfizer/BioNTech) is a third-generation, nucleic acid (mRNA) based vaccine, which contains the mRNA of the spike protein as active ingredient. The entrance of the molecule into the cells near the site of the inoculation is helped by different stabilizing additives and adjuvants (polyethylene glycol, lipids). The mRNA is translated by the protein synthetizing system of the cells following the penetration, and the synthetized spike protein provokes an immune response.
- 3. The mRNA-1273 (produced by Moderna) works on a similar basis, but the ingredients used for stabilization and absorption of the active compound are different.
- 4. AZD1222 (produced by Oxford/AstraZeneca) is a vector based vaccine; the cDNA of the coronaviral spike protein is inserted into the genome of an adenovirus vector (chimpanzee adenovirus, ChAdV) penetrating into the cells, which synthetize the spike protein. Two doses of the vaccine are used for immunisation.
- 5. SputnikV (produced by Gamaleya) works on a similar basis, but this vaccine uses two different human adenoviruses (HAdV5 and

HAdV26) in the first and second dose to transfer the spike protein gene into the cells.

6. Jcovden (produced by Johnson&Johnson/Janssen) is also a vector vaccine, but reaches the basic immunisation with a single dose. Its vector is also a human adenovirus (HAdV5).

Vaccine side effects may appear in a certain number of cases and in different forms.²² These are sometimes natural reactions at the site of the injection following the inoculation (local pain, swelling, and erythema). Another portion is natural, even if unpleasant, and is caused by the enhanced activity of the immune system. Some of these are general symptoms, reactions of the whole body (fever, shivers, fatigue and weakness, headache, joint and muscle pains) or localized to the injection site. Inappetence, nausea, swollen and painful axillary lymph node rarely may appear. A very rare but life threatening adverse reaction is the anaphylactic shock, which is an allergic overreaction resulting in breathing difficulties, collapse of the blood circulation, unconsciousness and occasionally death. Adverse effects lasting for several weeks or even months were also reported (skin alterations, rushes, myocarditis, tachycardia, thromboembolism, hormonal misbalances in women). Medical consultation is strongly recommended in these cases.

Covid-19 vaccine hesitancy must also be mentioned, since it could be observed in rather high portions of the population,²³ and as a consequence the vaccination rate remained under 70% in Hungary, while in several West-European countries it exceeded 90%. This concerned the law enforcement organizations in two respects. On the one hand, they had to take actions against the too aggressively demonstrating "anti-vaxxers". On the other hand, vaccine scepticism also appearing within the law enforcement organizations represented risks. Vaccination rates within these bodies did not exceed the rate observed within the population, even if vaccination was

²² Source: https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting

²³ Chevallier, C., Hacquin, A.-S., Mercier, H. (2021): COVID-19 Vaccine Hesitancy: Shortening the Last Mile. Trends in Cognitive Sciences, 25, 331-333

obligatory in a certain period. Deadlines for getting vaccinated were repeatedly postponed, and finally cancelled; therefore it remained unanswered whether these forces could have maintained their operability in all areas (police work, prison guarding, disaster recovery, fire guard and border patrol system) if the vaccine sceptic members had rather left the service then got vaccinated. This problem needs a solution even in the future if obligatory mass immunization may become necessary, either in case of a new pandemic or due to bioterrorist attacks. It must also be emphasized that the law enforcement and disaster management workers are usually second on the list of the vaccine action plans in most countries, right after health care system workers. Had that been so in Hungary, these forces would have faced the problem much sooner, in the first months of 2021. If vaccination is not obligatory, the high number of diseased staff, if it is obligatory, the high number of dismissed and quitting staff may paralyze these organizations, representing a risk in maintaining operability when the demand is the highest.

Conclusions

We may presume, based on the knowledge accumulated during the Covid-19 pandemics and other coronaviral epidemics that the SARS-CoV-2 will become endemic in most countries of the World. It means that it is constantly present in the population of a certain country, and every autumn, in the season of respiratory infectious diseases, we can expect the emergence of the SARS-CoV-2 also in Hungary. Common cold, influenza and Covid-19 will be observed simultaneously. Whether this constant presence will cause epidemic waves periodically or will appear in the form of occasional sporadic cases among the population is still in question.

We can deduce that three epidemic waves have caused high mortality and strain on the health care system in Hungary up to now: the second wave in the autumn of 2020, the third in the spring of 2021, and the fourth in the autumn of 2021. The first and the fifth waves were less significant, although during the latter the number of infections was high. Despite the fact that at the peak of the fifth wave on 20th of January 2022 the number of the daily registered infections exceeded twenty thousand (0.2% of the population), it strained the health care system less than the fourth wave. In this respect the third wave (caused by the alpha variant) was the most critical, the number of hospitalized people, the number of patients needing intensive care and the number of Covid-19 casualties were the highest during the third wave.

The differences in the identification of casualties as "Covid casualties" do not change the disadvantageous position of the so called post-Soviet countries in the statistics. The next table shows the top ten states on the list of the countries suffering the highest losses to the Covid-19 pandemic from its beginning till 23rd June, 2022. Nine of the ten countries are in the post-Soviet region.²⁴

	Country	Covid-19 casualties/1M in- habitants	
1.	Peru	6,300	
2.	Bulgaria	5,438	
3.	Bosnia and Herze- govina	4,875	
4.	Hungary	4,851	
5.	Northern-Macedo- nia	4,475	
6.	Montenegro	4,334	
7.	Georgia	4,237	
8.	Croatia	3,955	
9.	Czech Republic	3,750	

²⁴ Source: https://www.worldometers.info/coronavirus

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10. Slovakia	3,685
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Another method is also used in the statistical analysis of the losses caused by the pandemic to evaluate the effect of Covid-19 due to the differences in the definition of the term "Covid-19 casualty". This is the so-called "excess mortality", which means comparison of the average mortality in the two total years of the epidemics (2020 and 2021) to the average mortality of the five years preceding the pandemic. This excess mortality was 14% in Hungary.²⁵ The top twelve countries in the European Union are listed in the next table. Nine of the top ten belong to the so-called post-Soviet countries.

	Country	Excess mortality (%)	
1.	Bulgaria	26	
2.	Poland	24	
3.	Slovakia	23	
4.	Romania	21	
5.	Czech Republic	20	
6.	Slovenia	17	
7.	Cyprus	15	
8.	Croatia	15	
9.	Lithuania	15	
10.	Hungary	14	
11.	Spain	14	
12.	Malta	14	

 $^{^{25}}$ Source: https://telex.hu/defacto/2022/05/31/sok-vagy-keves-embereletet-vesztettunk-covidban

The data show that Hungary performed rather poorly in both evaluations. The causes of these high losses should be investigated (sociological reasons, level of public health standards, health destroying lifestyle and habits, health education etc.). It must be emphasized that the countries of the so called post-Soviet region (including Hungary) are overrepresented according to both statistical evaluation methods (number of Covid-19 casualties per one million inhabitants and excess death rate).

We can conclude that the infectivity of SARS-CoV-2 has increased by time due to the mutations, while its virulence has decreased significantly. Accordingly, at present the introduction of obligatory vaccination is not necessary among law enforcement organizations, teachers, public service workers etc. Furthermore, it would raise resistance and protests among them. Since in the last year the health risks decreased markedly, presumably no general restrictions will be necessary (curfew, obligatory online-education, travel restrictions etc.) in the future and Covid-19 vaccination will be optional in the population, similarly to flu control. Consequently, the documentation of immunity to SARS-CoV-2 will not be compulsory to run a normal life. More and more people will prefer getting reconvalescent immunity and vaccination will be necessary only in the risk groups. Voluntary immunisation should be offered in campaigns, mostly in autumns in the season of respiratory infections, giving a chance to get immunized against flu, Covid-19 and pneumococcal pneumonia.

While in Europe the decision makers concluded that the population has to learn to live together with SARS-CoV-2, some countries chose different strategies. The "zero Covid strategy" of China is in greatest contrast with the European approach. "zero Covid strategy" is very difficult to maintain for economic and social psychological reasons, and means a surplus burden on the health care system and law enforcement organizations due to growing public resistance. In the long run coexistence with the virus seems to be more feasible.

Mutants emerging in the future must be intensely monitored; their significance depends mainly on the changes in infectivity and virulence. The tendencies and consequence of changes in these characteristics are summarized in the next table.

Infec- tivity	Viru- lence	Consequence to the population
De- creases	De- creases	Beneficial , since SARS-CoV-2 will become alike the four previously known, classical corona- viruses causing common cold.
In- creases	De- creases	Beneficial , because the new variant will immun- ize more people through natural infection without causing severe illness and without causing a strain to the health care system.
De- creases	In- creases	Indifferent , because a less infective variant may not become dominant over the present omicron mutant, and dies out soon.
In- creases	In- creases	Hazardous , but the population is at least partially immune (vaccination, reconvalescence) so the risk is negligible.

Anyhow, the pandemic has proven the vulnerability of society and economy based on globalisation, since the previous way of life, economy, tourism and global trade still has not been restored after two years, either on local (national) or on global levels. It gave a chance to the law enforcement forces, health care workers, decision makers and, most of all, to the population to face the epidemic situations, handle and recover from other disasters, even at the cost of heavy sacrifices. Several conclusions can be drawn by these actors, including the law enforcement forces, regarding the control of epidemics. First of all, we cannot be sure that the next pandemics will be caused by a relatively mild pathogen causing losses mainly among elderly people suffering mostly from chronic health problems. A microorganism causing foethopathy, paediatric disease, haemorrhagic fever or encephalitis would represent a much higher risk and imperil children, pregnant women and active, working people, hence may cause panic. The consequences of vaccine hesitancy may be much more severe in the case of such a pathogen both among the population and within the law enforcement forces. There would be hardly enough time to convince anti-vaxxers following a deliberately generated bioterrorist action with a highly pathogenic, genetically modified microorganism to ensure the efficacy of the necessary control measures. The Covid-19 pandemic was useful as an exercise and to evoke attention; the health care workers, the decision makers, the media workers, the population and also the law enforcement forces passed the exam more or less successfully, though the rather poor position of our country in the international statistics shows that there is room for further development. The experiences gained by the handling of the Covid-19 pandemic were good to call our attention to the problems which should be taken care of, in order to overcome similar situations in the future.