Rationale for classification of SARS-CoV-2 virus into risk group 3 with the supplement “Z”

Background:

Several cases of a new form of respiratory diseases were described for the first time in the Chinese city of Wuhan (Hubei Province, People's Republic of China) in December 2019.

All patients were reported of having previous contact to a food market in Wuhan where fish, marine and other wild animals were marketed. The disease progresses in some patients with severe pneumonia and was officially designated “Coronavirus Disease 2019” (COVID-2019) by the WHO on 11 February 2020. Taking into account the data reported in February 2020, the mortality rate was estimated to be around 2 percent of the infected patients. Based on the sequencing of the virus genome that was isolated from the patients, the International Committee on Taxonomy of Viruses (ICTV) identified the pathogen as a new representative of the Coronaviridae family and assigned it to the subgenus Sarbecovirus (under the subfamily Orthocoronavirinae, genus Betacoronavirus). The data showed over 96 percent sequence identity to SARS-like coronaviruses that had been detected in bats (Bat-SL-CoVZC45, Bat-SL-RaTG13). Together with these, the new human coronavirus was classified as type 2 of SARS-CoV (severe acute respiratory syndrome-related coronavirus, SARS-CoV-2).

SARS-CoV-2 has shown to be a pathogen causing a systemic infection that can be accompanied by severe pneumonia. In addition, micro-infarcts and damage to the vascular system, the kidneys and other organs, which are probably caused by the infection of the endothelium, can also develop in persons suffering from COVID-19. High concentrations of SARS-CoV-2 have been detected in infected persons’ respiratory air. Particularly in enclosed spaces the viruses are transmitted very efficiently from person to person by droplets and aerosols and then spread throughout the population. Infected persons can emit and transmit SARS-CoV-2 already before developing symptoms (fever, cough, pneumonia); infected persons not having any symptoms or showing only mild, cold-like symptoms also transmit the pathogen. This has contributed to a very fast pandemic spread of SARS-CoV-2 infections. Globally, the number of persons who have been diagnosed and registered with a SARS-CoV-2 infection was almost 55 million (54,418,895) as of 16 November 2020; the number of deaths registered in this group is 1,317,707 (Johns Hopkins University). This corresponds to a case fatality rate of 2.42 %. The number of infections reported in Europe (EU, including the UK) is more than 10 million (10,560,273), 265,184 of those infected have died, this corresponds to an average case fatality rate of 2.51 %. This rate differs across countries - it ranges from 0.8 % (Austria), 1.2 % (Denmark) and 1.6 % (Germany) to 2.7 % (Belgium), 2.8 % (Spain) and 3.9 % (Italy, United Kingdom). The statistical data have been taken from the overview of the Johns Hopkins University, U.S. [15] and the ECDC, Sweden [17]. The proportion of deaths among infected persons reported in Germany between the end of July and the beginning of October 2020 was less than 1 % and significantly lower compared with the
incidence in spring [13, RKI, Täglicher Lagebericht (daily situation report) on 28 September 2020]. Since October 2020, the number of new infections has significantly increased across all German Länder compared to the summer. The Federal Statistical Office (destatis.de) now uses the term of excess mortality, in particular, regarding people with an age of 80 years and more. In October 2020, the mortality rates were for example 4 % above the average of previous years (www.destatis.de). Even though the case fatality rate had hardly changed in the course of this “second wave” until mid-November, it cannot be ruled out that the recently increased proportion of over 60-year-olds among the newly infected persons may lead to a renewed increase in the number of death cases in the coming weeks [13, RKI, Täglicher Lagebericht am 15.11.2020].

Different reasons might attribute to the reduction in the case fatality rate observed since the beginning of the pandemic:

(I) Younger persons are being currently infected, most of whom are less likely to become seriously ill.

(II) More tests are being carried out with the effect that more milder or asymptomatic cases are detected.

(III) Clinics and physicians' offices gained increasing experience in treating COVID-19 patients, and treatment options are available for those with severe disease.

In addition, it has to be taken into account, that death cases occur in a time-staggered manner (often approximately 3 to 4 weeks after the people got infected). In the event of an increase in the number of infections, the ratios for the numbers of cases/deaths are shown in a distorted manner.

As for “reverse zoonoses”, SARS-CoV-2 infections are found in various pets, for example in cats and, very rarely, in dogs [23, 24, 25]. The infections are mostly asymptomatic in animals. Transmission is possible through virus-containing aerosols excreted by persons infected with COVID-19. Infected cats can also transmit SARS-CoV-2 to other cats. Infections have also been described in a number of further animal species such as minks and ferrets, while pigs and birds are considered to be not susceptible [26, 27]. While “re-transmissions” to humans have not been reported for infected domestic cats, it is assumed that a zoonotic “re-transmission” of infected minks back to humans is possible in individual cases [28].

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SARS-CoV-2 is similar to SARS-CoV-1, which, as a human-pathogenic representative of the subgenus Sarbecovirus, triggered the 2002/2003 SARS epidemic (mortality rate: 9.6 percent). The 2019-SARS-CoV-2 virus is also similar, albeit to a lesser extent, to MERS-CoV (Subgenus Merbecovirus), which, as the causative agent of the Middle East respiratory syndrome, causes severe lung disease (mortality rate of 34 percent), especially amongst people in the Arabian Peninsula states. As airborne transmittable viruses, SARS-CoV 1 and MERS-CoV, that cause infections leading to considerable morbidity and to a significant case fatality rate, are classified into risk group 3. Due to its similarity in molecular biology, the current epidemiological and clinical data as well as the unavailable options for treatment and vaccination, as well as the effective spread in the population, as is also the case for SARS-CoV-1 and MERS-CoV, SARS-CoV-2 is also assigned to risk group 3. Molecular biological studies of SARS-CoV-2 genetic material (sequence analyses) indicate, that closely related viruses occur naturally in certain bats. The most closely related Beta coronaviruses are SARS-CoV-1 (here again, bats are the typical reservoir hosts), MERS-CoV (natural hosts are dromedary camels) and further coronaviruses in
bats. So far, dogs, cats, rabbits, golden hamsters and ferrets have proven susceptible to SARS-CoV-2. It was not possible to infect guinea pigs with the virus. Nevertheless, there are no indications at the time of writing, that domestic animals such as dogs and cats play a major role in spreading SARS-CoV-2. Denmark, but also the Netherlands, Sweden, Italy, Spain and the United States of America have reported infections in minks in fur farms caused by humans infected with SARS-CoV-2. In the Netherlands, there is evidence of at least two infections of persons associated with mink farms. As SARS-CoV-2 had been spreading to more farms, the Netherlands and Denmark have decided to cull the animals. This measure helps, on the one hand, to fight an epizootic disease, but also to protect humans from being infected by the zoonotic pathogen SARS-CoV-2. SARS-CoV-2 is therefore an infectious agent transmissible between animals and humans, and, consequently, the infection it causes belongs to the group of zoonoses. Therefore, the pathogen has to be marked with “Z” [29].

There is no scientific information available justifying the classification of SARS-CoV-2 as a pathogen of risk group 4. According to the definition of risk groups and the national guideline TRBA 450 “Criteria for the classification of biological agents” [22], the severity of disease progression has to be considered explicitly. Pathogens causing severe diseases in practically all infected persons with a high case fatality rate of over 30 percent are classified into risk group 4. This is the case e.g. for hemorrhagic fevers (e.g. Ebola, Marburg, South American hemorrhagic fever, [21]). In the case of COVID-19, the situation is clearly different:

(I) Not all infected individuals develop serious symptoms and there is a clear indication that specific categories of patients are more affected. Data from the Robert Koch-Institute show that nationwide 86 percent of those who died from COVID-19 were 70 years old or older. The average age of death was 82 [16].

(II) And, as to be expected in this age group, almost all of the deceased persons suffered from comorbidities such as overweight, coronary heart diseases, asthma, COPD, diabetes mellitus type 2, peripheral arterial or neurodegenerative diseases [20].

(III) Furthermore, it is to be assumed that a considerable proportion of those infected with SARS-CoV-2 do not develop any illness or only mild, cold-like symptoms. A first study from North Rhine-Westphalia (Heinsberg) shows data indicating that the number of actually infected persons was about ten times higher than the number of persons identified and registered by a laboratory diagnosis. A study estimates the proportion of infected persons registered at 9.2 % [18]. Thus, the number of actually infected persons is 11 times higher than that of persons reported as infected. A similar result was shown for the COVID-19 outbreak on board the cruise ship Diamond Princess in spring 2020. 712 out of 3,711 persons on board the cruise ship (passengers and staff) were found to be infected of whom 410 (58 %) had no symptoms on the day they were tested [19]. It can therefore be assumed that a large proportion of those infected with SARS-CoV-2 do not become ill or do not become seriously ill.

(IV) The mainly airborne transmission of SARS-CoV-2 can also be prevented effectively by the proper use of personal protective equipment (incl. respiratory protection).

The latest epidemiological data also confirm the classification of SARS-CoV-2 into risk group 3. Due to the current epidemiology and clinic of COVID-19, a classification into risk group 4 is not scientifically justifiable. The classification into risk group 3 will be reconsidered as soon as sufficient vaccination or medical treatment options are available.
Literature:


12. Streeck H et al. Infection fatality rate of SARS-CoV-2 infection in a German community with a super-spreading event https://www.medrxiv.org/content/10.1101/2020.05.04.20090076v1

Committee on Biological Agents (Ausschuss für Biologische Arbeitsstoffe, ABAS) – www.baua.de/abas


16. Robert Koch-Institut, Fallzahlen: https://www.rki.de/DE/Content/InfAZ/N/Neuartiges_Coronavirus/Fallzahlen.html


