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### **Primary prevention of COVID-19: advocacy for vaccination from a neurological perspective**

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## **Introduction**

Immunization by means of vaccination is a global health success story, saving millions of lives every year. In this regard, the epidemiology of measles, rabies, polio, rubella, varicella, influenza and mumps infections, all of which can harm the nervous system, could be contained by global vaccination campaigns (1). In addition, toxoid vaccines against bacterial toxins such as tetanus and diphtheria are indispensable and effective interventions for toxin-mediated neurologic diseases (1). The use of conjugate vaccines against major causes of bacterial meningitis (e.g. *Haemophilus influenzae* type b, *Neisseria meningitidis*, and *Streptococcus pneumoniae*) in routine pediatric immunization programs as well as for high risk groups, have significantly lowered the burden of disease over the past three decades (2). Immunization against measles is the only preventive measure against subacute sclerosing panencephalitis (SSPE), a chronic progressive inflammatory disorder of the brain which is associated with a devastating course (3).

Prophylactic vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and the resulting coronavirus disease 2019 (COVID-19) is an eagerly awaited measure to contain the pandemic, which has had devastating medical, economic, and social consequences.

### **Impact of COVID-19 on neurology and patient care: 10 points**

Apart from the unprecedented consequences coronavirus disease 2019 (COVID-19) on global health care, neurological aspects need to be emphasized in further detail. Ten points which depict key issues with regard to neurology and patient care are listed below. The list is not exhaustive and will need to be updated in the further course of the pandemic.

1. Many of our patients fall into high risk categories for unfavorable course and outcome for COVID-19 by virtue of age, gender and presence of comorbidities (4).
2. The major acute neurological conditions reported in the context of COVID-19 are encephalopathy (hypoxic, septic, metabolic and acute hemorrhagic necrotizing) and cerebrovascular diseases (5, 6). Further manifestations include but are not limited to neuroinvasive disease as well as para- and postinfectious conditions of the central (e.g. acute disseminated encephalomyelitis) and peripheral nervous system (e.g. Guillain-Barré syndrome) (7).
3. Concerning reports of longer-term complications are being conveyed. Many patients with COVID-19 continue to complain of persistent symptoms, most of which are neurological in nature (8). These may include sequelae from injury to the central and peripheral nervous system as well as a wide spectrum of symptoms termed “post-COVID-19 syndrome” (9).
4. Neurological complications of COVID-19, while rare, are also observed in neonates, children and adolescents (10, 11). The analysis of 121 decedents of COVID-19 younger than 21 years revealed preexisting medical disorders in 75%. The most frequently reported conditions were chronic lung disease, neurologic and developmental conditions, and cardiovascular disorders (12).
5. Individuals with neurological comorbidity suffer from a more severe disease course with higher rates of ICU admission and significant mortality (13-15).
6. Individuals with preexisting neurological disorders and COVID-19 are at risk for exacerbation of neurological disease, e.g, dementia, Parkinson’s disease and epilepsy (16).
7. COVID-19 has an impact on decisions regarding the treatment of non-COVID-19 related neurological disorders, especially those with an immune-mediated background (17).

8. Social distancing and periods of shutdown impose a limitation for care, access and support of patients with acute and chronic neurological conditions such as cerebrovascular conditions, dementia, epilepsy, migraine, multiple sclerosis, Parkinson's disease, neuromuscular disorders, and more (17, 18).
9. No compromise can be made for adherence to the main pillars of primary prevention including physical distancing, wearing a mask, keeping rooms well ventilated, avoiding crowds, cleaning the hands, and coughing into a bent elbow or tissue. The possibility to adhere to these preventive measures may be limited in people with acute and chronic neurological conditions.
10. The pandemic has significant impact on mental health and is associated with neuropsychiatric sequelae (19).

### **Vaccination against SARS-CoV-2: the key measure to end the pandemic**

Currently, primary prevention strategies are based on reducing the risk of person to person spreading. Measures include physical or social distancing, quarantining, ventilation of indoor spaces, covering coughs and sneezes, hand washing, and keeping unwashed hands away from the face. Furthermore, the use of face masks or coverings is essential in public settings to minimize the risk of transmissions. These measure will be amended by the introduction of vaccines after the completion of Phase III trials and approval by the respective regulatory agencies (20). On December 21 2020, the European Medicines Agency recommended granting a conditional marketing authorization for the vaccine Tozinameran (Comirnaty®), an RNA vaccine, to prevent COVID-19 in people from 16 years of age (21). Applications for further vaccines have have been filed and approvals are expected to follow in early 2021. The vaccine for the pediatric population is still under development. Just vaccinating adults would not be enough to end the pandemic since children will likely serve as a reservoir of the virus, making it harder to end the pandemic. Moreover, continued research and development will be needed to stay ahead of potentially consequential viral mutations, which could have negative consequences for COVID-19 vaccines.

Regardless of the target antigen of the vaccine, the duration of the immunity conferred and the applied technology, this approach to establish protective immunity must be seen as the turning point to effectively combat the pandemic in the short and long run. Of note, vaccines exert two related but distinct functions. On the one hand they protect the vaccinated individual against the infection and on the other hand they promote herd immunity. The latter is based on the concept of disease control by lowering the

number of individuals who can spread the disease. Such immunity can be acquired naturally or induced by vaccination (22).

### **The fight against COVID-19 from a public health perspective**

All therapeutic interventions have potential risks. In this regard, there is overwhelming medical evidence from large scale and well-designed studies to show that negative side effects of vaccination are rare and minor. Vaccines are at special surveillance since they are administered to large and mostly healthy populations including infants and children (23). The low tolerance for risks needs to be carefully weighed against the benefits such an intervention which can prevent, reduce and even eliminate illness (24).

Vaccine safety is assessed from inception through the entire duration of its use. Extensive post-licensure surveillance will be diligently undertaken for the COVID-19 vaccine in order to identify adverse events and maintain a favorable risk benefit ratio (25). Obstacles to vaccination include concerns about vaccine safety and side effects, lack of trust, social norms, exposure to rumors and myths, and access barriers (26). The vaccine-hesitancy movement has contributed to dangerous resurgences of diseases such as measles which had been largely contained (27). The underlying issues of vaccine hesitancy are complex. Some contributing factors may be controlled in part by transparency and establishment of public confidence in vaccine safety and effectiveness. Neurologists are at the forefront of patients at risk and trusted sources. They can critically contribute to achieving individual and population immunity by supporting public health campaigns aimed at high vaccine uptake by informing, explaining and encouraging.

### **Statement by the NeuroCOVID-19 Task Force of the European Academy of Neurology**

There are now vaccines to prevent more than 20 life-threatening diseases, and work is ongoing at unprecedented speed to also make COVID-19 a vaccine-preventable disease. The impact of COVID-19 vaccines on the termination of the pandemic will depend on how many people get vaccinated and how quickly this can be carried out on a worldwide scale. The EAN Neuro-COVID-19 Task Force strongly supports a primary prevention strategy on the basis of vaccination and encourages neurologists to support the implementation. Priority groups for first vaccination will need to be defined and may include elderly people, healthcare workers and individuals with comorbidities. We make a plea that patients with chronic neurological disorders should have high priority for early access to the vaccine and emphasize the need to ensure global and equitable allocation.

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JS drafted the manuscript, critical revision by TJ, TVO and EM, further revision and intellectual contribution from all authors, approval from all authors.

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