


# Children with Epilepsy in the Era of COVID-19 Pandemic

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After the first report of several cases of pneumonia of unknown causes that resulted in acute respiratory distress syndrome in Wuhan, China in December 2019, a novel coronavirus was identified as the causative agent.<sup>1</sup> This was the seventh strain of human coronaviruses and was later named severe acute respiratory syndrome coronavirus 2 by the World Health Organization, and the disease caused by it was called coronavirus disease 2019 (COVID-19).<sup>2</sup> On March 11, 2020, the World Health Organization declared COVID-19 to be a pandemic.<sup>2</sup> Although the COVID-19 virus can infect human beings from the newborn period to old age, fortunately this virus affects children less frequently than adults, has no severe signs and symptoms, and also has lower morbidity and mortality. Unfortunately, it seems that COVID-19 is going to live with us at least until an effective vaccine becomes available, which is estimated to be over a year in an optimistic view. Therefore, pediatric neurologists have to modify their previous routine practices to provide appropriate care to patients against this potentially life-threatening infection.

Epilepsy is one of the most frequent neurologic disorders in children. Although the majority of patients with childhood-onset epilepsy attain remission, about one-third of these children develop antiseizure drug (ASD) resistance and need more sophisticated measures including surgery.<sup>3</sup>

Immunologic abnormalities have been reported in epilepsy either by direct effect of epilepsy on the immune system or by effect of ASDs on serum immunoglobulin levels.<sup>4–6</sup> There are several reports concerning the effects of ASDs therapy on humoral and cellular immunity. Several documented studies have shown that antiepileptic drugs can decrease serum immunoglobulin levels in children treated with ASDs.<sup>7–10</sup> The most common reported reduced immunoglobulin is

immunoglobulin (Ig)A, especially with phenytoin treatment. Carbamazepine and sodium valproate are also associated with changes in both humoral and cellular immunity. Furthermore, some studies reported that the reduction of serum immunoglobulins caused by ASDs is associated with increased susceptibility to recurrent infections. Ashrafi et al measured serum IgA, IgG, and IgM levels in a cohort of epileptic patients compared with age and gender-matched controls. This study indicated that ASDs could reduce serum immunoglobulins, especially IgA and IgG; among them, the carbamazepine effect is of more concern.<sup>6</sup> There were few studies about ASDs effects on serum IgG subclasses. IgG subclass deficiency induced by ASDs predisposes patients to specific infections, whereas asymptomatic patients were also reported.

One of the main issues in children with epilepsy, especially those with drug resistance, is anticonvulsant therapy and the possible interactions between antiseizure medications and the agents that might be used for the treatment of COVID-19 in these patients. Fortunately, a practical manual addressing this concern has been produced and frequently updated by the Liverpool Drug Interaction Group (based at the University of Liverpool, United Kingdom), in collaboration with the University Hospital of Basel (Switzerland) and Radboud University Medical Center (Netherlands).<sup>11</sup> On page 7 of this manual, the interactions between anticonvulsants and the agents that might be used in the treatment of COVID-19 have been explained. This manual (last updated: April 9, 2020) could be very useful when we need to administer ASDs or to change their dosages in COVID-19 patients. Moreover, no evidence-based recommendation could be found around this issue of how often patients should go to their neurologist for control during this pandemic.

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Until now, no study has shown that children with epilepsy without any health problems and easily controlled seizures seem to have a higher risk of getting coronavirus. Children with epilepsy who suffer from health problems like swallowing dysfunction, drooling, chest deformities, and those taking benzodiazepine are at a larger risk for respiratory infections that might put them at higher risk for COVID-19. In addition, in some epileptic syndromes taking medicines for controlling seizures may affect the immune system such as adrenocorticotrophic hormone, steroids, and immunotherapies. Moreover, 30% of children with epilepsy are drug-resistant and need rational polytherapy with ASDs that have already been shown to lead to humoral immunosuppression.<sup>4-6</sup> Therefore, it is highly likely that a proportion of children with drug-resistant epilepsy, such as those with concurrent health problems, may be at higher risk of developing more severe symptoms with viral illnesses like COVID-19.

In contrast to our opinion around the children with epilepsy, especially those with concurrent health problems and those with drug resistance, Professor Ley Sander—the Medical Director at the Epilepsy Society in the United Kingdom—has different opinions for patients with epilepsy.<sup>12</sup> We, authors of this article, appreciate his comments and we think that many people with epilepsy need to consider his recommendations. However, we believed that there are many unanswered questions about COVID-19 in children with epilepsy and it is logical that we would have concerns about these patients.

In conclusion, potentially a proportion of the children with epilepsy, especially those with concurrent health problems and drug-resistant epilepsy, may be at higher risk in the era of COVID-19. Therefore, it is indicated that all the child neurologists and caregivers do apply official guidelines to reduce the chance of COVID-19 in these vulnerable children.

#### Conflict of Interest

None declared.

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