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Epilepsy and COVID-19: Management of Patients and Optimization of Antiepileptic Treatment in the Pandemic

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There are as yet no data pointing to any increase in the incidence of the novel coronavirus infection (COVID-19) or a more severe course of illness in patients with epilepsy. However, considering the high prevalence of epilepsy in patients over 60 years of age, the high comorbidity of epilepsy and a whole series of somatic diseases, and the need to maintain the opportunity for constant access to antiepileptic medications and follow-up of epilepsy patients, we can expect a whole set of difficulties in the management of these patients in the conditions imposed by the COVID-19 pandemic. This article addresses the main principles of the management of epilepsy patients in the conditions of the COVID-19 pandemic: the need to follow regimes; preservation of regular and continuous taking of antiepileptic drugs, including consideration of interdrug interactions; and switching patients to i.v. forms of antiepileptic drugs where necessary.

Keywords: COVID-19, SARS-CoV-2, epilepsy, treatment adherence, antiepileptic drugs, interdrug interactions.

The state in the world in April 2020 was that number of cases infected with SARS-CoV-2, the pathogen of the novel coronavirus infection (COVID-19), was more than two million. In most cases, the disease occurs as a mild acute respiratory viral infection. However, when extremely severe and severe forms occur, further deterioration in a patient's well-being can occur very quickly, over periods of a few hours, because of the development of bilateral pneumonia, acute respiratory failure, acute respiratory distress syndrome, sepsis, and septic (infective-toxic) shock. World experience is that the most severe forms of the disease develop in patients aged 50 or more, who often suffer from cardiovascular diseases, diabetes mellitus, chronic obstructive pulmonary disease, and other chronic pathologies requiring continuing use of medications [1–4].

Neurological Manifestations of COVID-19. SARS-Cov-2 virus has been shown to enter cells by binding to angiotensin-converting enzyme 2 (ACE2) receptors, which are present in diverse organs and tissues, including pulmonary alveolar cells, the heart, kidneys, gastrointestinal tract, and the CNS, making the brain a potential target for the virus [5]. The ability of one member of the coronavirus family, SARS-CoV, to enter the brain via the olfactory epithelium and induce neuron death was demonstrated in transgenic mice [6] and, judging from the common hyposmia in COVID-19 patients, is also characteristic of SARS-CoV-2 [7].

Increases in the number of observations of patients with severe and extremely severe COVID-19 had led to increasing numbers of reports of the neurological manifestations of coronavirus infection. Thus, information obtained from retrospective studies of data from 214 hospitalized patients with COVID-19 (41.1% with severe signs) indicate that neurological symptoms were recorded in 36.4% of patients, more often in severe cases [8]. This relates primarily to symptoms of CNS involvement – headache, vertigo, impaired consciousness, ataxia, and some cases developing acute cerebrovascular accidents (aCVA), as well as one case of epileptic seizures; hyposmia, decreased taste sensitivity, and musculoskeletal symptoms were also noted.

A retrospective study reported by Li et al. [9] found that of 221 patients, 11 developed ischemic stroke, one ve-

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nous sinus thrombosis, and one hemorrhagic aCVA. The risk group for the development of stroke included elderly patients, those with comorbid pathology, and those tending to develop marked inflammatory responses and hypercoagulation. Another published study with a smaller number of observations indicated that that commonest neurological symptoms were vertigo, headache, and decreased levels of consciousness [10].

Asadi-Pooya and Simani, in their systematic review of the CNS signs of COVID-19 [10], pointed to a number of inadequacies in the studies addressed: the lack of targeted studies of neurological symptoms and lack of data on analysis of cerebrospinal fluid, electroencephalography, etc. Meanwhile, every day sees the appearance of new reports on possible rare (at least currently) neurological manifestations of the new coronavirus infection – viral meningitis/encephalitis [11], Guillain–Barré syndrome [12], and others, supporting the ability of the pathogen to damage the nervous system [13].

Thus, we have good grounds to expect the development of neurological symptoms in COVID-19 patients, particularly in older patients and those with severe disease and comorbid pathology.

Epilepsy Patients – a COVID-19 Risk Group? Data from the International League Against Epilepsy, the Epilepsy Society, and the Epilepsy Foundation, as well as the Association of British Neurologists and other sources, indicate that the risk of patients developing the novel coronavirus infection in epilepsy patients corresponds to that of the general population [14]. Epilepsy patients do not show any tendency to more severe disease, except for people with weak respiratory muscles and low mobility and those with marked bulbar impairments [14, 15].

It is important to note that there is a series of rare forms of epilepsy in which patients are particularly vulnerable to increases in body temperature or who need hormone therapy (Dravet syndrome, etc.). A good but sad example may be provided by the recent death at age 13 years of Charlotte Figi in the USA with Dravet syndrome and significant developmental delay, who became the heroine of a CNN story about early use of cannabinoids leading to a sharp reduction in the number of seizures and an improvement in the rate of development [16]. The girl was hospitalized in April 2020 with pneumonia, probable COVID-19, impaired breathing, and seizures; sadly, she died [17]. In Dravet syndrome with COVID-19 infection, as in any other acute respiratory viral infection with elevated temperature, the possibility of increasing the dose of previously prescribed antiepileptic drugs (AED) should be considered, in the meantime using antipyretic drugs (preferably paracetamol, though it should be emphasized that at present there is no evidence that paracetamol has any advantages over ibuprofen) [18].

The group at risk of severe disease included people aged over 60 years, where the prevalence of epilepsy is known to be higher than in the younger adult population. Considering the high somatic comorbidity of epilepsy and a whole series of diseases (cardiovascular disease, lung disease, diabetes mellitus, strokes, etc.) [19–22], there are grounds for expecting a more severe course of disease in patients with epilepsy and comorbid somatic pathology.

Increases in Stress Levels and the Problem of Treatment Adherence. Epilepsy patients not infrequently have comorbid pathologies, including psychiatric [20, 22–24], and they have a greater tendency to form suicidal ideations and a greater frequency of suicide attempts [25]. In the Russian population, the number of epilepsy patients with depression, affective-anxiety, and other disorders is very high, though as shown by our observations, a majority of these patients avoid seeing a psychiatrist [22].

The COVID-19 pandemic is a significant stress factor, especially for patients with chronic diseases which require following daily regimes and constant taking of medications. The epidemiological situation has caused them to miss planned visits to their treating physicians. Stress levels increase significantly when patients have to self-isolate and all the more so when an epilepsy patient contracts the novel coronavirus infection.

There is presently a number of widespread chronic diseases in which treatment success is based on following a regime including regular taking of medications by patients [26]. However, the problem of low treatment adherence is often an insurmountable obstacle to success. In 2003, the WHO developed guidelines for improving treatment adherence in patients with various chronic diseases and states requiring prolonged drug therapy: bronchial asthma, oncological diseases, depression, diabetes mellitus, epilepsy, HIV/AIDS, hypertension, tobacco addiction, and tuberculosis [27]. Adherence to long-term treatment in the WHO draft is taken to mean the extent to which a person's behavior – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider [27].

The WHO takes the view that it is the patient's agreement with treatment that distinguishes the concept of "treatment adherence" from that of "compliance" and to some extent is taken as a synonym of "treatment adherence," though in clinical practice use of both terms is acceptable.

WHO data indicate that when the guidelines were created, in 2003, long-term adherence in patients with these chronic diseases in countries with high income levels was at a level of about 50%, and was even lower in developing countries. Malek et al. [28], in their review, found levels of adherence failure ranging from 26% to 79%.

In the situation of sharp changes in sleep and rest regimes, elevated stress loads, difficulties with the availability of hospital care, particularly when self-isolating, problems with treatment adherence can arise even in the most disciplined patients. Epilepsy patients should follow advice common to all guidelines: not to focus on negative information, to preserve their daily routine and social circle as

much as possible, to pay attention to physical loads, and to occupy their free time with educational and recreational electronic and media resources. It is extremely important to avoid alcohol intake, sleep deprivation, and other causes of increased attack frequency, to continue ongoing use of AED in accordance with medical advice, to avoid planned visits to the epilepsy specialist if there is no increase in attack frequency or severity, not to alter the treatment scheme, and in cases of deterioration of wellbeing to call an ambulance to determine the need for hospital admission.

In 2005, Lai et al. [29] published results from a study of cases in which patients with epilepsy terminated AED therapy during the previous SARS epidemic in 2003. Of 227 patients, 49 stopped treatment. Of these 49 patients, 28 developed seizures, these being serious in four cases and constituting status epilepticus in two cases. As might be expected, seizures due to withdrawal of AED arose primarily in patients with symptomatic epilepsy and polytherapy and not in medication-induced remission.

Continuing regular intake of AED is particularly important for patients with epilepsy infected with the novel coronavirus as, despite only occasional reports of seizures on the background of infection, the situation in these patients can deteriorate due to toxicity, elevated temperature, and general degradation of status (especially on development of severe forms), interdrug interactions with drugs used for the treatment of COVID-19, the need to switch patients from tablet AED to other formulations and sometimes other AED when patients have to be put on mechanical ventilation of the lungs (MVL).

The Need to Consider Interdrug Interactions. The treatment of patients with epilepsy, especially those infected with the novel coronavirus, requires extremely strict adherence to ongoing treatment schemes. However, some cases may require correction of therapy, which has to be carried out individually with agreement of a neurologist (epileptologist). The Solov'ev Scientific and Applied Psychoneurological Center has compiled and published methodological guidelines, "Treatment of Patients with Epilepsy in the COVID-19 Pandemic," and has organized a telephone rota of epileptologists to allow possible questions to be answered actively [30].

The treatment of COVID-19 in the Russian Federation currently uses a series of drugs: antivirals, antimalarials, and antibacterials. Clinical trials of novel drugs have been undertaken and attempts to transfuse plasma from convalescent patients have been made. A continuous international exchange of advice and experience in the use of drugs has taken place. Current and constantly updated information on interdrug interactions between drugs used in the treatment of COVID-19 in different countries can be found on a website [31]. Our published guidelines include a table with data to March 24, 2020 (Table 1), and at the time of writing there is an update from April 9, 2020 (Table 2).

It should be noted that significant changes were made to the table over a period of two weeks: some drugs for the treatment of the novel coronavirus infection (probably those not displaying adequate efficacy, such as darunavir) and some AED were removed from the table, while warnings of potential cardiotoxicity regardless of the type of AED used simultaneously were introduced with regard to lopinavir + ritonavir, chloroquine, and hydroxychloroquine [32]. Information on some AED (for example, lacosamide) was revised. The research group emphasizes that the information is constantly updated and that data on some drugs is limited or missing, and that risk must be assessed in each case individually.

Several AED – carbamazepine, oxcarbazepine, eslicarbazepine, phenytoin, phenobarbital, primidone, and rufinamide – are potential inhibitors of drugs used for the treatment of the novel coronavirus infection. Appendix 5 of the Temporary Methodological Guidelines of the Russian Federation Ministry of Health (version 5, April 8, 2020) indicates that carbamazepine, phenobarbital, and primidone should not be used alongside lopinavir + ritonavir and must not be taken simultaneously with chloroquine and hydroxychloroquine. In these cases, and also when there are increases in seizure frequency, switching patients to other AED can be considered (preferably those from the group with minimal potential interdrug interactions) (see Tables 1 and 2) after consultation with a neurologist (epileptologist) [30].

In relation to some AED, data have been obtained on possible increases in the area under the concentration-time curve on the background of treatment with antiviral and antimalarial drugs. Data have been obtained indicating that tocilizumab may have such an effect on the concentration-time curves of various AED, which can lead to decreases in their efficacy (see Tables 1 and 2). At the same time, there are some AED which have not yet been seen to have interdrug interactions with agents used in the treatment of COVID-19. These include (data of April 9, 2020) gabapentin, lacosamide, levetiracetam, pregabalin, retigabin, topiramate, vigabatrin, and zonisamide. These drugs (with the least potential interdrug interactions) should be given preference when there is a need for first prescription of AED in patients with COVID-19.

It is important to take account of the possibility of cumulative cardiotoxic and hepatotoxic actions of various AED and drugs for the treatment of COVID-19 when used together.

Where there is a need to use benzodiazepines, the possibility of developing or exacerbating respiratory failure [30] must be remembered.

The temporary methodological guidelines of the Russian Federation Ministry of Health (version 5, April 8, 2020) for etiotropic therapy of the novel coronavirus infection suggest using chloroquine, hydroxychloroquine, lopinavir + ritonavir, and azithromycin (in combination with hydroxychloroquine, as there are data indicating increased antiviral effects with this substance when used in this drug combination), mefloquine, and interferon formulations. Umifenovir, remdesivir, and favipiravir are currently in clinical trials.

TABLE 1. Clinically Significant Interdrug Interactions between AED and the Main Drugs Used in Treating Patients with COVID-19 (data on March 24, 2020)

	ATV	*DRV/c[1]	*LPV/r	RDV[2]	FAVI	CLQ	HCLQ	NITA	RBV	TCZ[3]	IFN-β-1a[4]	OSV
Brivaracetam	↔	↔	↓	↔	↔	↑	↑	↔	↑	↔	↔	↔
Carbamazepine	⇓↑	⇓↑	⇓↑	⇓	↔	⇓	⇓	↔	↔	⇓↓	↔	↔
Cannabidiol	↔	↑	↑	↔	↔	↑	↑	↔	↔	↔	↔	↔
Cenobamate	⇓	⇓	⇓	↔	↔	⇓	⇓	↔	↔	↔	↔	↔
Clonazepam	↑	↑	↑	↔	↔	↔	↔	↔	↔	↔	↔	↔
Clobazam	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
Diazepam	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
Eslicarbazepine	⇓♥	⇓	⇓♥	⇓	↔	⇓	⇓	↔	↔	↔	↔	↔
Ethosuximide	↑	↑	↑	↔	↔	↔	↔	↔	↔	↔	↔	↔
Felbamate	↓	⇓	↓↔	↔	↔	↓♥	↓♥	↔	↔	↔	↔	↔
Gabapentin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
Lacosamide	↔♥	⇑	↔♥	↔	↔	↔	↔	↔	↔	↔	↔	↔
Lamotrigine	↔	↑	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔
Levetiracetam	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
Lorazepam	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
Oxcarbazepine	⇓	⇓↓	⇓	⇓	↔	⇓	⇓	↔	↔	↔	↔	↔
Perampanel	↑	⇓	↑	↔	↔	↔	↔	↔	↔	↔	↔	↔
Phenytoin	⇓	⇓	⇓	⇓	↔	⇓	⇓	↑	↔	↓	↔	↔
Phenobarbital	⇓	⇓↓	⇓	⇓	↔	⇓	⇓	↔	↔	↓	↔	↔
Pregabalin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
Primidone	⇓	⇓	⇓↓	⇓	↔	⇓	⇓	↔	↔	↓	↔	↔
Retigabin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
Rufinamide	⇓	⇓	⇓	⇓	↔	⇓	⇓	↔	↔	↔	↔	↔
Sulthiame	↑	↑	↑	↔	↔	↔	↔	↔	↔	↔	↔	↔
Tiagabine	↑	↑	↑	↔	↔	↔	↔	↔	↔	↔	↔	↔
Topiramate	↔	⇓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
Sodium valproate	↔	⇓	⇑	↔	↔	↔	↔	↔	↔	↔	↔	↔
Vigabatrin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
Zonisamide	↔	↑	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔

* Use only in combination with booster drugs (ritonavir or cobicistat). ATV – atazanavir; DRV/c – darunavir/cobicistat; LPV/r – lopinavir/ritonavir; RDV – remdesivir/GS-5734; FAVI – favipiravir; CLQ – chloroquine; HCLQ – hydroxychloroquine; NITA – nitazoxanide; RBV – ribavirin; TCZ – tocilizumab; IFN-β-1a – interferon-β-1a; OSV – oseltamivir. [1] Johnson & Johnson, which owns Janssen Pharmaceutica, which releases darunavir, has now reported a lack of evidence for the efficacy of schemes based on darunavir in the treatment of SARS-CoV-2. [2] Some data on drug interactions of remdesivir are not currently available. [3] Increases in IL-6 concentrations, as with other cytokines, can lead to increases in the plasma drug concentrations because of reductions in liver metabolism (CYP-associated), while treatment with tocilizumab (anti-IL-6R) can decrease the plasma concentrations of previously given drugs due to normalization of liver metabolism. [4] Studies on interdrug interactions have not been performed in humans. ↑ – potentially increases the effect of AED (increases the area under the condition-time curve); ↓ – potentially decreases the effect of AED (decreases the area under the condition-time curve); ⇑ – potentially increases the effects of drugs for the treatment of COVID (increases the area under the concentration-time curve); ⇓ – potentially decreases the effects of drugs for the treatment of COVID (decreases the area under the concentration-time curve); ↔ no effect on each other; ♥ – one or both drugs leads to increases in QT and/or PQ.

Drugs should not be prescribed together.

Potential interdrug interactions may require dose correction or careful monitoring.

Potential interdrug interaction very likely to be minor, additional monitoring measures or dose correction probably not needed

Clinically significant interactions not expected

TABLE 2. Clinically Significant Interdrug Interactions between AED and the Main Drugs Used in Treating Patients with COVID-19 (data on April 9, 2020)

	ATV	LPV/r ♥	RDV	FAVI	CLQ ♥	HCLQ ♥	RBV	TCZ	IFN-β
Carbamazepine	⇓↑	⇓↑	⇓	↔	⇓	⇓	↔	↓	↔
Clonazepam	↑	↑	↔	↔	↔	↔	↔	↔	↔
Eslicarbazepine	⇓	⇓	⇓	↔	⇓	⇓	↔	↔	↔
Ethosuximide	↑	↑	↔	↔	↔	↔	↔	↔	↔
Gabapentin	↔	↔	↔	↔	↔	↔	↔	↔	↔
Lacosamide	↔	↔	↔	↔	↔	↔	↔	↔	↔
Lamotrigine	↔	↓50%	↔	↔	↔	↔	↔	↔	↔
Levetiracetam	↔	↔	↔	↔	↔	↔	↔	↔	↔
Oxcarbazepine	⇓	⇓	⇓	↔	⇓	⇓	↔	↔	↔
Perampanel	↑	↑	↔	↔	↔	↔	↔	↔	↔
Phenobarbital (phenobarbitone)	⇓	⇓	⇓	↔	⇓	⇓	↔	↓	↔
Phenytoin	⇓	⇓	⇓	↔	⇓	⇓	↔	↓	↔
Pregabalin	↔	↔	↔	↔	↔	↔	↔	↔	↔
Primidone	⇓	⇓↓	⇓	↔	⇓	⇓	↔	↓	↔
Retigabin	↔	↔	↔	↔	↔	↔	↔	↔	↔
Rufinamide	⇓	⇓	⇓	↔	⇓	⇓	↔	↔	↔
Sulthiame	↑	↑	↔	↔	↔	↔	↔	↔	↔
Tiagabine	↑	↑	↔	↔	↔	↔	↔	↔	↔
Topiramate	↔	↔	↔	↔	↔	↔	↔	↔	↔
Valproic acid	↔	⇑38%*	↔	↔	↔	↔	↔	↔	↔
Vigabatrin	↔	↔	↔	↔	↔	↔	↔	↔	↔
Zonisamide	↔	↔	↔	↔	↔	↔	↔	↔	↔

ATV – atazanavir; LPV/r – lopinavir/ritonavir; RDV – remdesivir; FAVI – favipiravir; CLQ – chloroquine; HCLQ – hydroxychloroquine; RBV – ribavirin; TCZ – tocilizumab; IFN-β – interferon-β. ↑ – potentially increases the effect of AED (increases the area under the condition-time curve); ↓ – potentially decreases the effect of AED (decreases the area under the condition-time curve); ⇑ – potentially increases the effects of drugs for the treatment of COVID (increases the area under the concentration-time curve); ⇓ – potentially decreases the effects of drugs for the treatment of COVID (decreases the area under the concentration-time curve); ↔ no effect on each other; ♥ – data from https://www.crediblemeds.org/ indicate that these drugs have or may have the ability to prolong QT or increase the risk of developing torsade de pointes (TdP) – ventricular tachycardia of the "pirouette" type – and this risk may increase with increases in the concentration or dose of the drug or on simultaneous use with drugs inducing similar effects [32]. *A single case in an initially stable patient requiring an increase in the sodium valproate dose.

Drugs should not be prescribed together.

Potential interdrug interactions may require dose correction or careful monitoring.

Potential interdrug interaction very likely to be minor, additional monitoring measures or dose correction probably not needed

Clinically significant interactions not expected

The Temporary Methodological Guidelines of the Russian Federation Ministry of Health (version 4 of March 27, 2020 and version 5 of April 8, 2020) indicate that in complicated cases of infection, various clinical situations may indicate the use of antibiotics, including various combinations, with different levels of proepileptic potential and different probabilities of interdrug interactions with AED [30, 33–35]:

1. Protected aminopenicillins (amoxicillin/clavulanate, amoxicillin/sulbactam): these can exacerbate epilepsy, though no interaction with AED has been described [34–37];

2. β-Lactam antibiotics with antopseudomonas activity (piperacillin/tazobactam, meropenem, imipenem/cilastatin, doripenem) and *carbapenems* can exacerbate epilepsy. Imipenem is more of an epileptogen than doripenem and meropenem. Decreases in valproic acid concentrations have been demonstrated on the background of treatment with carbapenems [34, 35];

3. Respiratory fluoroquinolones (levofloxacin, moxifloxacin) can exacerbate epilepsy, though therapeutically significant interactions with AED have not been described [34 35];

4. 3rd-, 4th-, and 5th-Generation cephalosporins (including combinations with macrolides) can in some cases exacerbate epilepsy, particularly in patients with renal failure; interactions with AED have not been described [34, 35];

5. Vancomycin (a tricyclic glycopeptide): exacerbation of epilepsy and interactions with AED have not been described [38];

6. Linezolid (oxazolidinones): postmarketing studies indicate that convulsions have been described in patients; it is suggested that simultaneous use with powerful liver enzyme inducers (carbamazepine, phenytoin, phenobarbital) can decrease exposure to linezolid [39];

7. Macrolides (particularly erythromycin but also clarithromycin and others): approved for use in patients with epilepsy, though simultaneous use with various AED, particularly *carbamazepine* and *valproic acid*, but also *oxcarbazepine*, may lead to increases in concentration, elevating the probability of developing toxic effects. These properties of macrolides are due to inhibition of cytochrome P-450 in the liver, though azithromycin is a weaker inhibitor than other macrolides and is less involved in interdrug interactions [33–35]. According to the Methodological Guidelines of April 8, 2020, azithromycin is the drug of choice for the treatment of COVID-19 patients, so its use in infected patients with epilepsy can be regarded as quite safe. However, simultaneous use with a number of AED requires the possibility of increases in their concentrations to be considered, with therapeutic monitoring where appropriate.

Thus, of this list of antibiotics, use of *protected aminopenicillins*, *carbapenems*, *respiratory fluoroquinolones*, and *cephalosporins* should as far as possible be avoided in epilepsy patients with COVID-19, or their possible proepileptic effects should be considered. Possible decreases in exposure to a number of antibiotics when used simultaneously with liver enzyme inducers should also be borne in mind. Most publications deal with interdrug interactions of antibiotics with carbamazepine and valproic acid, though there are few data for newer AED, so where prescription of antibiotics to epilepsy patients is necessary it is important to check for increases in the frequency or severity of seizures (possible consequences of reduced AED concentrations) and signs of toxicity – drowsiness, vertigo, double vision, changes in blood biochemistry, the ECG, etc. (possible results of increased AED concentrations).

Published data indicate that the highest expectation of deterioration in the situation in terms of seizures and the occurrence of various side effects is in patients with impaired renal function and elderly patients [34]. Monitoring of blood AED levels and consultation with a neurologist (epileptologist) are required in situations of concern.

Where first prescription of AED is required in patients with COVID-19, preference should be given to drugs with the lowest potential for interdrug interactions: levetiracetam, zonisamide, pregabalin, and others (see Tables 1 and 2).

The Epilepsy Patient: Hospitalization and Treatment in Hospital Conditions. Indications for hospitalization of epilepsy patients include deterioration of wellbeing due to infection and increases in the severity of the situation regarding epileptic seizures. In addition, the de novo development of epileptic seizures in hospital conditions in patients with severe disease can occur in relation to elevated body temperature, development of viral encephalitis, the existence of an inherited predisposition, and histories of other factors for the development of epilepsy.

The recommendations of leading epileptologists indicate that when there are no increases in the severity or frequency of seizures, patients should continue their ongoing AED in tablet form. Patients are switched to i.v. forms when tablets cannot be taken (impaired swallowing, need to transfer patient to MVL, etc.) and should take account of interdrug interactions (see Tables 1 and 2); patients are returned to p.o. formulations when the situation stabilizes [30].

I.v. formulations of valproates, levetiracetam, and lacosamide are currently registered in the Russian Federation, though the latter has restricted areas of use as it is indicated as adjunctive therapy only for focal seizures accompanied or not accompanied by secondary generalization in patients with epilepsy aged 16 years and above [40, 41].

Management of patients with serial seizures in status epilepticus in the emergency department is by an emergency specialist working alongside a neurologist [30].

Conclusions. Increases in the numbers of confirmed cases of SARS-CoV-2 infection, given the trend towards more severe disease in elderly patients and those with comorbid pathologies, will unavoidably increase the number of patients with chronic diseases regularly taking a variety of drugs and likely to develop acute states requiring an individual approach. In conditions of the increasing load on doctors due to patients with the novel coronavirus infection, healthcare provision by experts with narrow specialties (epileptologists, movement disorder specialists, and so on) is particularly important in terms of developing clear advice regarding the treatment of patients with epilepsy, Parkinson's disease, neuromuscular diseases, etc., with the possibility of remote consultations. The International League Against Epilepsy has created the ILAE COVID Task Force international working group, whose work involves the world's leading epilepsy specialists. Webinars are provided in the framework of the Epicare program; two webinars including European epileptologists and Professors E. Perucca, E. Trinka, S. Shorvon, and others have addressed the work of epilepsy departments and the difficulty of managing patients with epilepsy in the COVID-19 pandemic [42]. Information for patients and doctors regarding the course and treatment of epilepsy in the pandemic is continuously updated [14], as are data on drug interactions [31, 32]; changes in the Temporary Clinical Guidelines of the Russian Federation Ministry of Health are updated. All these efforts are directed

to maintaining the efficacy of care for epilepsy patients in the COVID-19 pandemic.

The authors have no conflicts of interests.

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