



Iranian Epilepsy Association

ILAE  
IRAN

# 18<sup>th</sup> International Epilepsy Congress of Iran

هجدهمین  
کنگره بین المللی صرع ایران



انجمن متخصصین مغز و اعصاب ایران

۶-۴ اسفند ماه ۱۴۰۰ 23-25 February 2022  
Tehran - Iran



ILAE  
EUROPE

## خلاصه مقالات

# Abstract Book



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دبیرخانه کنگره: تهران، میدان توحید، ابتدای خیابان توحید، بین  
خیابان نصرت و برجم، پلاک ۶، طبقه دوم  
تلفن: ۶۶۱۲۵۹۱۶

دارای امتیاز بازآموزی برای:  
متخصصین مغز و اعصاب، روان پزشکان، جراحان مغز و اعصاب،  
فوق تخصص اعصاب اطفال، پزشکان عمومی

**In the name of God**

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**Dr. Hossein Pakdaman**

*Congress president  
Professor of Neurology  
Shahid Beheshti University of Medical Sciences  
President of the Iranian Neurology Association*

Thank God for the success of holding the "18th International Epilepsy Congress of Iran" despite the all problems particularly the COVID-19 pandemic.

This year, with the great attendance of professors of neurology both in Iran and abroad and cooperation of the Iranian neurology association, Iranian Epilepsy Association, Iranian chapter of ILAE and sincere attendance of Dr. Nasim Tabrizi as the chairperson, 18th IECI will be held semi-virtually. Although, in recent years a significant progress has been made in updating the information of the Iranian neurologists, efforts to promote the scientific advance to the highest level will continue.

Current condition and social problems of epilepsy in Iran, updates in management of epilepsy in children and adults, New diagnostic and treatment methods, neuroimaging, drug-resistant epilepsy, etc.", are among the main and significant topics in this congress. We hope that the cooperation and assistance of experienced professors interested in these topics, makes the congress useful and fruitful. Finally, I would like to thank the organizers of this congress, whom their great efforts, have made this program more magnificent.



**Nasim Tabrizi**

*Congress chairperson*

*Associate professor of neurology, fellowship in epilepsy  
Mazandaran University of medical sciences*

On behalf of the Iranian chapter of International League Against Epilepsy (ILAE) and Iranian epilepsy association, it is my pleasure to welcome you to 18<sup>th</sup> international epilepsy congress of Iran (IECI). Although, the covid-19 pandemic has limited the opportunity to meet in person, we have gotten the chance to enhance our relationships with the other expert colleagues all over the world, by virtual communication methods. The scientific program of 18<sup>th</sup> IECI has covered many aspects of epileptology with the most focus on recent advances in diagnosis and management of epilepsy which are certainly necessary to address special issues of daily practice.

The sessions will be held in two parallel virtual halls simultaneously, with the feasibility of concurrent translation to English for the Persian sessions. Three teaching sessions are also scheduled including seizure semiology, EEG interpretation and management of epilepsy.

There is a competition for neurologists at the first day of congress which will challenge their knowledge on epileptology. The winners of competition will be awarded in the closing ceremony. Moreover, the first three young Iranian researchers in epileptology which have sent their CVs during the previously determined period, will be appreciated at the final day.

I hope this congress brings you enjoyable and beneficial learning experiences along with useful exchange of ideas.

## Scientific committee

Sanaz Ahmadi, MD  
Marjan Asadollahi, MD  
Shervin Badv, MD  
Majid Ghafarpour, MD  
Kurosh Gharagozli, MD  
Hossein Pakdaman, MD  
Behnam Safarpour, MD  
Sohrab Hashemi Fesharaki, MD  
Jafar Mehvari, MD  
Mahmoud Mohammadi, MD  
Mahmoud Motamedi, MD  
Seyyed Navid Naghibi, MD  
Dariush Nasabi Tehrani, MD

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# Scientific program

# 18<sup>th</sup> International Epilepsy Congress of Iran

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فوق تخصصی اعصاب اطفال، پزشکان عمومی



Wednesday 23 February 2022

**Hall A****8-8.40: Welcome-Opening ceremony****Targeting epilepsy in special groups.1**

Co-chairs: Hossein Pakdaman, Belal Adibeig, Parviz Bahrami

<i>Time</i>	<i>Title</i>	<i>Speaker</i>
8.40-9.5	The global burden and care of epilepsy in Iran	Hossein Pakdaman
9.5-9.30	Pharmacotherapy of epilepsy in elderly	Mahmoud Motamedi
9.30-9.55	How to diagnose and treat post-stroke seizure and epilepsy	Kurosh Gharagozli
9.55-10.20	Update on treatment of low-grade epilepsy associated tumors	Dariush Nasabi Tehrani
10.20-10.45	Advances in pharmacotherapy of sleep-related epilepsy	Mohammad Reza Najafi
10.45-11	Panel discussion	

**Update on pharmacological therapies in epilepsy**

Co-chairs: Mahmoud Motamedi, Dariuosh Savadi Osgouei

<i>Time</i>	<i>Title</i>	<i>Speaker</i>
11 -11.20	Novel pharmacological therapies for epilepsy in the pipeline	Mohammad Zare
11.20-11.40	Diuretics and epilepsy	Majid Ghafarpour
11.40-12	Management of pharmacokinetic interactions of anti-seizure medications in comorbidities	Abbas Tafakhori
12-12.20	The influence of genetic variants on response to anti-seizure medications	Hamideh Arvan
12.20-12.40	Pharmacogenetic of adverse events caused by anti-seizure medications	Farzad Sina
12.40-13	Therapeutic drug monitoring for new generation anti-seizure medications	Behnam Safarpour
13-13.20	How to optimize treatment and what can go wrong?	Parviz Bahrami
13.20 - 13.40	Panel discussion	

**Ronak symposium**

Chair: Jafar Mehvari

<i>Time</i>	<i>Title</i>	<i>Speaker</i>
14-14.30	Valproate in the treatment of epilepsy and status epilepticus	Hossein Kahnouji
14.30-15	Continued importance of valproate for women with generalized epilepsy	Mahyar Noorbakhsh

**Neuroimaging.1**

Co-chairs: Elham Rahimian, Abtin Doroudinia

<i>Time</i>	<i>Title</i>	<i>Speaker</i>
15.30-16	PET and SPECT in non-lesional drug resistant epilepsy: Considerations and pitfalls	Abtin Doroudinia
16-16.30	Ultra-high field MRI in epilepsy: Clinical application	Gaurav Verma
16.30-17	The role of diffusion tensor imaging in drug-resistant epilepsy	Luis Concha
17-17.30	MRI-derived biotyping in epilepsy	Andrea Bernasconi & Neda Bernasconi

17.30-18	Panel discussion
Wednesday 23 February 2022	

## Hall B

### Psychosocial issues in epilepsy

Co-chairs: Afshin Samaei, Hossein Ali Ebrahimi, Mohsen Pour Kakroudi

<i>Time</i>	<i>Title</i>	<i>Speaker</i>
8.40-9	Costs and socio-economic aspects of epilepsy care	Dariush Nasabi Tehrani
9-9.20	Legal rights and issues in epilepsy	Mohammad Ali Emam Hadi
9.20-9.40	Quality of life and stigma in patients with epilepsy	Nahid Ashjazadeh
9.40-10	How to improve the life of patients with epilepsy?	Mehran Homam
10-10.20	How to do clinical research on epilepsy? Challenge for young investigators	Soheila Rezakhani
10.20-10.30	Panel discussion	
10.20-11	Neurologist competition	Navid Naghibi

### Teaching session: EEG/ECG

Co-chairs: Mahmoud Mohammadi, Sohrab Hashemi Fesharaki, Navid Naghibi

<i>Time</i>	<i>Title</i>	<i>Speaker</i>
11-11.20	Misleading non-epileptic epileptiform activities on scalp EEG recordings	John M. Stern
11.20-11.40	Common pitfalls in interpretation of EEG	William O. Tatum
11.40-12	Standardized critical care EEG terminology: 2021 version	Marjan Asadollahi
12-12.20	Is this a spike? Operational criteria for defining interictal epileptiform discharges	Sanaz Ahmadi
12.20-12.40	Important biophysical and technological aspects of EEG for clinical applications	Hossein Kahnouji
12.40-13	What can happen to the heart during video EEG recordings?	Rainer Surges
13-13.20	Panel Discussion	

### MRI-negative epilepsy

Co-chairs: Jafar Mehvari, Mehdi Soltani

<i>Time</i>	<i>Title</i>	<i>Speaker</i>
15-15.30	Optimizing lesion detection- pitfalls	William Theodore
15.30-16	Optimizing lesion detection - higher field MRI and advanced methods	Paolo Federico
16-16.30	Next steps- candidates for surgery	Fernando Cendes
16.30-17	Surgical outcome and need for re-operation	Walter J. Hader
17-17.30	Panel discussion	

Thursday 24 February 2022

**Hall A****Pediatric epilepsy**

Co-chairs: Reza Azizi Mal Amiri, Jafar Nasiri, Omid Yaghini

<i>Time</i>	<i>Title</i>	<i>Speaker</i>
8-8.20	Update on treatment of childhood epilepsies	Mahmoud Mohammadi
8.20-8.40	Novel and de novo mutations in pediatric refractory epilepsy	Reza Shervin Badv
8.40-9	Inborn errors of metabolism and epilepsy: diagnosis, and treatment approaches	Mahmoud Reza Ashrafi
9-9.20	Update on treatment of developmental and epileptic encephalopathies	Reza Azizi Mal Amiri
9.20-9.40	Post-surgical outcome in pediatric patients with drug-resistant epilepsy	Mohammad Barzegar
9.40-10	Classification of seizures and the epilepsies in neonate	Ronit M. Pressler
10-10.30	Panel discussion	

**Epilepsy and fertility**

Co-chairs: Marjan Asadollahi, Navid Naghibi

<i>Time</i>	<i>Title</i>	<i>Speaker</i>
10.30-11	Anti-seizure medication exposure in infants of breastfeeding mothers with epilepsy	Navid Naghibi
11-11.30	Reproductive disorders in women with epilepsy: The role of anti-seizure medications	Erik Taubøll
11.30-12	Valproate in treatment of epilepsy in girls and women of childbearing potential	Torbjörn Tomson
12-12.30	Management of epilepsy during pregnancy and postpartum	Kimford J. Meador
12.30-13	The neurodevelopmental outcomes of treatment with newer anti-seizure medications in pregnancy	Rebecca Louise Bromley
13-13.30	Panel discussion	

**KMT symposium**

<i>Time</i>	<i>Title</i>	<i>Speaker</i>
13.30-14	CBD in epilepsy: Current practice	Farzad Sina
14-14.30	CBD: Is it a new antiseizure medication?	Reza Shervin Badv

**Nonconvulsive status epilepticus**

Co-chairs: Mehdi Soltani, Farzad Sina, Behnam Safarpour

<i>Time</i>	<i>Title</i>	<i>Speaker</i>
15-15.30	The epidemiology of nonconvulsive status epilepticus	Boulenouar Mesraoua
15.30-16	Nonconvulsive status epilepticus: etiology, clinical features and prognosis	Peter W. Kaplan
16-16.30	Pharmacotherapy for nonconvulsive status epilepticus	<a href="#">Lawrence J. Hirsch</a>
16.30-17	The EEG diagnosis of nonconvulsive status epilepticus, challenges in clinical application	Réjean M. Guerriero
17-17.30	Panel discussion	

Thursday 24 February 2022

**Hall B****Novel therapies in epilepsy**

Co-chairs: Sanaz Ahmadi, Mana Ahmadian

<i>Time</i>	<i>Title</i>	<i>Speaker</i>
8-8.30	Closed loop system in drug-resistant epilepsy	Esther Krook-Magnuson
8.30-9	Antiepileptogenesis and disease modifying therapy	Terence O'Brien
9-9.30	From trial and error to precision medicine	Samuel Wiebe
9.30-10	Focused ultrasound for drug-resistant epilepsy	Hsiang-Yu Yu
10-10.30	Targeting the gut-brain axis for treatment of epilepsy	Nasim Tabrizi
10.30-11	The genetics of pharmacoresistance in mesial temporal lobe epilepsy	Iscia Lopes-Cendes
11-11.30	Panel discussion	

**Targeting epilepsy in special groups.2**

Co-chairs: Vahid Salehifar, Reza Azizi Mal Amiri, Gholamreza Shamsaei

<i>Time</i>	<i>Title</i>	<i>Speaker</i>
11.30-11.55	Updates on management of autoimmune epilepsy	Vahid Salehifar
11.55-12.20	Management of epilepsy caused by nodular heterotopia	Mahyar Noorbakhsh
12.20-12.45	Management of epilepsy caused by focal cortical dysplasia	Saeid Charsuei
12.45-13.10	Updates on management of epilepsy in tuberous sclerosis complex	Nicola Specchio
13.10-13.30	Panel discussion	

**Neuroimaging.2**

Co-chairs: Marjan Asadollahi, Elham Rahimian

<i>Time</i>	<i>Title</i>	<i>Speaker</i>
15.30-16	MRI essentials in epileptology	Elham Rahimian
16-16.30	Neuroimaging in focal epilepsy	John S. Duncan
16.30-17	Neuroimaging in psychogenic non-epileptic events	Markus Reuber
17-17.30	Neuroimaging of dual pathology and double pathology	Yahya Aghakhani
17.30-18	Panel discussion	

Friday 25 February 2022

**Hall A****Case-based discussion**

Co-chair: Mohammad Reza Najafi, Mohammad Zare, Dariush Nasabi Tehrani

<i>Time</i>	<i>Title</i>	<i>Speaker</i>
8.30-8.50	Lesional mesial temporal lobe epilepsy	Roshanak Tirdad
8.50-9.10	Non-lesional mesial temporal lobe epilepsy	Nayyereh Akbari
9.10-9.30	Bitemporal lobe epilepsy	Jafar Mehvari
9.30-9.50	Lesional neocortical epilepsy	Sohrab Hashemi Fesharaki
9.50-10.10	Non-lesional neocortical focal epilepsy	Sanaz Ahmadi
10.10-10.30	Multiple pathologies	Babak Bakhshayesh
10.30-10.50	Extensive lesion/malformation of cortical development	Samaneh Haghghi
10.50-11	Panel discussion	

**Status epilepticus**

Co-chairs: Sanaz Ahmadi, Hossein Kalani, Hossein Kahnouji

<i>Time</i>	<i>Title</i>	<i>Speaker</i>
11-11.30	Optimizing status epilepticus management during the COVID-19 pandemic	Asieh Mehramiri
11.30-12	Consensus definition for NORSE	Nicolas Gaspard
12-12.30	Novel pharmacological therapies for refractory and super-refractory status epilepticus	Francesco Brigo
12.30-13	Neurostimulation in treatment of refractory and super-refractory status epilepticus	Eugen Trinka
13-13.30	Panel discussion	

**Cobel Darou symposium**

<i>Time</i>	<i>Title</i>	<i>Speaker</i>
13.30-14:30	Rational polytherapy: Levetiracetam & lacosamide	Farzad Sina

**Iranian chapter of ILAE**

<i>Time</i>	<i>Title</i>
14.30-15.30	The report of constituent's members and conferring about upcoming election

**EEG/MEG**

Co-chairs: Marjan Asadollahi, Reza Azizi Mal Amiri

<i>Time</i>	<i>Title</i>	<i>Speaker</i>
15.30-16	Understanding and management of ictal-interictal continuum	Marjan Asadollahi
16-16.30	Update on the role of magnetoencephalography in refractory epilepsy	Umesh Vivekananda
16.30-17	EEG in the diagnosis and classification of the epilepsy syndromes: clinical practice in adult	Fatemeh Yourdkhani
17-17.30	Panel Discussion	

**17.30-18: Closing ceremony- Acknowledgment and award giving**

Friday 25 February 2022

**Hall B****New ways for seizure detection**

Chair: Mehdi Soltani

<i>Time</i>	<i>Title</i>	<i>Speaker</i>
8-8.30	SUDEP- risk factors and prevention	Mehdi Soltani
8.30-9	Seizure detection devices, where are we?	Sándor Beniczky
9-9.30	Future aspects of using outpatient long-term monitoring	Jonas Duun-Henriksen

**Teaching session: Seizure semiology**

Chair: Reza Shervin Badv

<i>Time</i>	<i>Title</i>	<i>Speaker</i>
9.30-10	Is this epilepsy? (Adult patients)	Jafar Mehvari
10-10.30	Epilepsy imitators (Pediatric patients)	Mohsen Javadzadeh
10.30-11	Panel discussion	

**Teaching session: Treatment of epilepsy**

Co-chair: Vahid Salehifar, Behnam Safarpour

<i>Time</i>	<i>Title</i>	<i>Speaker</i>
11-11.25	Selecting anti-seizure medication in new-onset epilepsy	Marjan Asadollahi
11.25-11.50	What if the first two drugs fail? Next level drug therapy	Sohrab Hashemi Fesharaki
11.50-12.15	Assessment of treatment efficacy: When to refer for pre-surgical evaluation?	Mana Ahmadian
12.15-12.40	Treatment withdrawal in drug-responsive epilepsy	Soheila Rezakhani
12.40-13.5	Treatment withdrawal after epilepsy surgery	Jafar Mehvari
13.5-13.30	Panel discussion	

**Hot topics in neuropsychiatry and neurosurgery**

Co-chairs: Houshang Moein, Majid Barkatain, Navid Naghibi

<i>Time</i>	<i>Title</i>	<i>Speaker</i>
15-15.20	Minimally invasive techniques in epilepsy surgery	Saadi Ghatan
15.20-15.40	Neurostimulation in drug-resistant epilepsy	Kristl Vonck
15.40-16	Predicting favorable outcome after epilepsy surgery	Mohsen Aghaei Hakkak
16-16.20	Long-term outcome of re-operation	Imad Najm
16.20-16.40	Cognitive disorders in patients with epilepsy	Majid Barkatain
16.40-17	Practice guideline for treatment of depression in adults with epilepsy	Marco Mula
17-17.30	Panel discussion	

# Oral Presentations

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## Neuroimaging of Dual/Double Pathology

**Yahya Aghakhani, MD, FRCPC**

*Director of the Epilepsy Program and EEG Lab, Clinical Associate professor of Neurology  
Section of Neurology, Department of Internal Medicine, University of British Columbia.*

So called dual pathology is not uncommon, up to %20 of patients with drug resistant focal epilepsy, which may cause some difficulties in seizure focus localization and planning of epilepsy surgery. This has been reported in various form of epileptogenic lesions, but the most frequently hippocampal sclerosis (HS) is seen in association with focal cortical dysplasia (FCD), particularly in temporal lobe. It is not always clear if HS is an epiphenomenon caused by frequent seizures or the initial insult or abnormality leads to HS. The more crucial question is the role of identified lesions including HS in patient's epilepsy. Intracranial video-EEG monitoring is usually required to answer this question. Based on the reported case series, having more than one epileptogenic lesion does not preclude a good surgical outcome. In fact, the outcomes are comparable with those patients who have single epileptogenic lesion. In general, a better surgical outcome could be achieved if both lesions are completely removed, but it should not be done or justified in every patient routinely as patients with preserved hippocampal function or lesion in eloquent area may experience a significant functional deficit after resection.



## Non-lesional mesial temporal lobe epilepsy

**Nayyereh Akbari, MD**

*Neurologist, Epilepsy fellowship.*

Prevalence of epilepsy was 1% and 30%-40 % of them fall in to Drug resistant epilepsy. They are candidate for epilepsy surgery and success rate of resective epilepsy surgery was 40-90%. TLE is more frequent (66%) focal epilepsy and 30 % of them has normal MRI. Mesial TLE is a network disorder and more extensive structural abnormalities within and beyond temporal and extratemporal cortex and white matter both ipsilateral and contralateral to H.S was described. Clinicopathological, structural and functional difference was known between HS positive-TLE and Normal MRI-TLE. MRI negative TLE is not subtle version of HSTLE or mild HS it is a separate condition which affect distinct brain network.

Negative MRI is highly dependent on imaging technique, magnetic field power and reviewers experience, so should be improved awareness.

Determination of epileptogenic network has important role in presurgical evaluation. To reach this goal we can use invasive technique such as intracranial EEG or less/noninvasive technique such as quantitate MRI, DTI, MRS, FMRI, MSI, Volumetric study, PET scan/SPECT coregistered with MRI, EEG-FMRI, HD-ESI, ECoG. 75-80% of patient with normal MRI and Hypometabolism on FDG-PET ipsilateral to EEG onset seizure, has excellent post-surgical (ATL) outcome. New option is investigated for whom that not candidate for resective surgery (e.g. DBS, RNS, MRgLITT).

## The influence of genetic variant on response to ASMs

**Hamide Arvan, MD**

*Assistant professor of neurology, Neurology research center, Kerman University of medical sciences, Kerman, Iran.*

Pharmacogenomics, i.e., the influence of genetic variants on drug response or adverse effects, bear the potential to support the choice of the most suitable ASMs. Genes can affect drug response influencing pharmacokinetic parameters by causing variable activity of the systems responsible for the metabolism and transport of the drug as well as influencing pharmacodynamics through drug targets.

Genetic influence on ASMs pharmacokinetics is primarily related to the polymorphism of enzymes involved in ASMs metabolism. CYP2C9/2C19 polymorphisms may be relevant in the metabolism/bioavailability of phenytoin, brivaracetam, CLB and partially valproate, as well as barbiturates, while UGT (UGT1A4 and UGT2B7) variants are associated with variable kinetics of lamotrigine and valproate.

Progress in genomic testing has resulted in identification of a large number of epileptic genes, which account for a large proportion of nonacquired epilepsies. Upon identifying the genetic basis of the disease, the treatment can be directed toward correction of specific metabolic defects such as conduction of ketogenic diet for glucose transporter-1 deficiency or pyridoxine use for pyridoxine-dependent epilepsies. Knowing the genetic basis of the disease can help in avoiding ASMs that can aggravate the pathogenic defect, such as sodium channel-blocking drugs in Dravet syndrome caused by mutation in SCN1A. However, in the treatment of early-onset epileptic encephalopathy due to glutamate ionotropic receptor NMDA-type subunit 2A (GRIN2A) missense mutation (L812M), memantine administration resulted in decreased seizure frequency.

No reliable gene marker of resistance to ASMs has been identified to date, although there are data suggesting the possible role of ABCB1 and ABCC2 gene variants. By analyzing several HLA alleles, we can identify high-risk individuals for development of SJS and TEN induced by CBZ, most important of which are HLAB\* 15:02 and HLAA\*31:01. Also, variant allele carriers have an increased risk in case of the use of OXC, phenytoin and lamotrigine.

## Selecting anti-seizure medication in new-onset epilepsy

**Marjan Asadollahi, MD**

*Associate Professor of Neurology, Fellowship in Epilepsy.*

In approaching to a patient with a new-onset seizure, first, it should determine whether it is a true epileptic seizure or a non-epileptic event. The next step is determining whether the seizure is provoked or unprovoked. If the seizure is unprovoked, does it fulfill the criteria of epilepsy and warrants long-term antiseizure medication (ASM). In selecting ASM, the patient's epilepsy type and co-morbid condition is a main concern. All the above issues will be discussed in detail.

## Understanding & management of interictal-ictal continuum (IIC)

**Marjan Asadollahi, MD**

*Associate professor of neurology, Fellowship in epilepsy.*

The IIC is synonymous with “possible electrographic seizure” or “possible electrographic status epilepticus.”

The IIC is a purely electrographic term that is NOT a diagnosis; it requires careful interpretation in the full clinical context. The pattern on the IIC, does not qualify as an electrographic seizure or SE, but there is a reasonable chance that it may be contributing to impaired alertness, causing other clinical symptoms, and/or contributing to neuronal injury. Thus, it is potentially ictal in at least some sense and often warrants a diagnostic treatment trial, typically with a parenteral antiseizure medication.

IIC is defined as any periodic discharge (PD) or spike-and-wave (SW) pattern, with frequency between 1.0 to 2.5 Hz lasting  $\geq 10$  seconds OR any PD or SW pattern that averages  $\geq 0.5$  Hz and  $\leq 1.0$  Hz over 10 seconds plus modifier or fluctuation or any lateralized rhythmic activity more than 1 Hz for  $\geq 10$  seconds with a plus modifier or fluctuation. This includes any Lateralized rhythmic delta activity (RDA), bilateral independent RDA, unilateral independent RDA, and multifocal independent RDA, but not generalized RDA.

Moreover, in this presentation, difference kinds of lateralized periodic discharges (LPDs) including interictal/irritative brain injury versus ictal/peri-ictal LPDs will be discussed.

## Standardized critical care EEG terminology: 2021 version

**Marjan Asadollahi, MD**

*Associate Professor of Neurology, Fellowship in Epilepsy.*

In this presentation, I will discuss about some of the important EEG terms, including Periodic and rhythmic discharges and its significance.

The two common EEG terms “evolution” & “fluctuation”. In summary, “evolution” in EEG means at least two unequivocal, sequential changes in waveform frequency, morphology, or location. “Fluctuation in EEG” means, three or more changes in frequency (by at least 0.5 Hz), morphology or location, but not qualifying as evolving.

“Electrographic seizure” is defined as either: epileptiform discharges more than 2.5 Hz for at least 10 seconds or any pattern with definite evolution, lasting at least 10 seconds.

“Electrographic status epilepticus” is defined as an electrographic seizure for more than 10 continuous minutes or for a total duration of  $\geq 20\%$  of any 60-minute period of recording.

“Electroclinical seizures” defined as: Any definite clinical correlate time-locked to the pattern (of any duration) or EEG and clinical improvement with intravenous antiseizure medication.

## **Inborn Errors of Metabolism and Epilepsy: Diagnosis, and Treatment Approaches**

**Mahmoud Reza Ashrafi, MD**

*Professor of Pediatric Neurology, Children's Medical Center, Tehran University of Medical Sciences.*

According to the World Health Organization, approximately 50 million people live with epilepsy around the world, with an estimated 2.4 million newly diagnosed people yearly. Inborn errors of metabolism are rare as individual entities, but their estimated combined incidence is 1 in 3000 live births. Seizures are common manifestations of many inborn errors of metabolism, especially in neonates, infants, and children. Neurometabolic disorders are not a frequent cause of epilepsy, but epilepsy is a frequent comorbidity in many Neurometabolic disorders.

Although IEMs are responsible for only a fraction of epileptics, it is imperative to identify them, as there is often treatment available, which can mitigate or even prevent major neurological sequelae. It is important to consider the possibility of an IEM in a patient presenting with seizures of an unknown cause not only due to the amenability to causal treatment of the seizures and the possible co-morbidities, but also in order to adequately perform genetic counseling and to more accurately predict the disease trajectory and prognosis.

Neurometabolic epilepsies can be classified according to different criteria, i.e., type of biochemical defects and clinical presentation. More recently the age of onset of metabolic epilepsy has been considered for classification.

It is important to consider the possibility of an IEM in a patient presenting with seizures of an unknown cause not only due to the amenability to causal treatment of the seizures and the possible co-morbidities, but also in order to adequately perform genetic counseling and to more accurately predict the disease trajectory and prognosis.

## Update on treatment of the developmental and epileptic encephalopathies

**Reza Azizi Malamiri, MD**

*Assistant Professor, Department of Paediatric Neurology, Golestan Medical, Educational, and Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.*

The brain is the most complex creature in the universe and many genes, proteins, pathways, and networks work together to give function to this complex creature. A normal brain not only does not seize but also leads to normal development. Patients with developmental and epileptic encephalopathies show developmental impairments because of two reasons; underlying etiology and frequent epileptiform activity. Almost all these developmental epileptic encephalopathies have a genetic basis from copy number variants with many involved genes to single nucleotide variants with just one base change. In many of these developmental and epileptic encephalopathies, the traditional approach to seizure management could lead to devastating results such as worsening of encephalopathy after administering sodium channel blockers to manage focal seizures in Dravet syndrome. In recent years and after increasing our knowledge of the genetic basis of developmental and epileptic encephalopathies and their underlying pathophysiologic mechanisms, the precision medicine approach to seizure management has revolutionized the outcome of these conditions. In this short talk, I will rapidly review the precision medicine approach in Dravet syndrome as the prototype of developmental and epileptic encephalopathies in children.

## Seizure detection devices, where are we?

**Sándor Beniczky**

*Department of Clinical Neurophysiology, Danish Epilepsy Center, Dianalund and Aarhus University Hospital, Aarhus, Denmark.*

The International League Against Epilepsy (ILAE) and the International Federation of Clinical Neurophysiology (IFCN) has recently published a clinical practice guideline (CPG) for healthcare personnel working with patients with epilepsy, in outpatient, ambulatory settings. The Working Group of the ILAE and IFCN developed the CPG according to the methodology proposed by the ILAE Epilepsy Guidelines Working Group. The working group reviewed the published evidence using The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement and evaluated the evidence and formulated the recommendations following the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. The group found high level of evidence for the accuracy of automated detection of generalized tonic-clonic seizures (GTCS) and focal-to-bilateral tonic-clonic seizures (FBTCS) and recommend the use of wearable automated seizure detection devices for selected patients when accurate detection of GTCS and FBTCS is recommended as a clinical adjunct. They also found a moderate level of evidence for seizure types without GTCS or FBTCS. However, it was uncertain whether the detected alarms resulted in meaningful clinical outcomes for the patients. The working group recommend using clinically validated devices for automated detection of GTCS and FBTCS, especially in unsupervised patients, where alarms can result in rapid intervention (weak/conditional recommendation). At present, they do not recommend clinical use of the currently available devices for other seizure types (weak/conditional recommendation). Further research and development are needed to improve the performance of automated seizure detection and to document their accuracy and clinical utility.



## Novel pharmacological therapies for refractory and super-refractory status epilepticus

**Francesco Brigo**

*Hospital Franz Tappeiner, Department of Neurology, Merano, Italy.*

*Department of Neuroscience, Biomedicine and Movement Sciences, University of Verona, Verona, Italy.*

Refractory status epilepticus (RSE) is a status epilepticus (SE) that continues despite first- and second-line treatments (i.e., benzodiazepine and intravenous antiseizure medications, respectively). Super-refractory SE (SRSE) is a SE continuing or recurring 24 h or more after the onset of anesthetic therapy, and includes cases of SE recurring on the reduction or withdrawal of anesthesia. Both are associated with high morbidity and mortality. The pharmacological treatment of RSE and SRSE is often regarded as an evidence-free zone, due to the lack of randomized controlled trials. Most data on the treatment of RSE/SRSE are obtained from observational studies, conducted in small and heterogeneous populations, and are therefore not informative, and prone to bias and confounding. The underlying etiology of RSE/SRSE should be promptly identified and adequately treated. Novel antiseizure medications, such as perampanel and topiramate, appear promising; their mechanisms of action and pharmacological properties should be carefully considered to optimize their effectiveness. In some patients with RSE, sequential trial(s) of antiseizure medications could lead to SE resolution; sometimes this strategy might represent an effective alternative to the use of anesthetics, a class of drugs associated with increased risk of infection and death. Ketamine, a noncompetitive NMDA receptor antagonist, could be effective in RSE/SRSE, considering the subcellular maladaptive changes that occur in these conditions. Within the intrinsic clinical heterogeneity of RSE/SRSE, distinct electroclinical phenotypes with different responses to pharmacological interventions were recently identified. This could represent the first step towards a tailored approach in the pharmacological treatment of these conditions.

## The neurodevelopmental outcomes of treatment with newer anti-seizure medications in pregnancy

**Rebecca Louise Bromley**

*Division of Evolution and Genomic Science, University of Manchester, Manchester, UK.  
Royal Manchester Children's Hospital, Manchester Academic Health Sciences, Manchester, UK.*

Prenatal exposure to certain antiseizure medications is associated with an increased risk of both congenital anomalies and longer-term neurodevelopmental difficulties. There is evidence that phenobarbital, valproate, carbamazepine and topiramate are associated with higher levels of physical and/or neurodevelopmental risk, highlighting that this is a class of medications to be carefully investigated.

This presentation focuses on the neurodevelopmental aspects of child outcome following in utero exposure to 'newer' antiseizure medications. Neurodevelopment is a term which refers to a set of skills which include cognitive, motor, social and behavioural functioning that expand over the childhood and adolescent years. An increased risk of significant and lifelong disruption to these neurodevelopmental trajectories was observed following exposure to valproate in utero, highlighting the importance of in-depth neurodevelopmental investigation.

In infancy children exposed to lamotrigine or levetiracetam appear to reach developmental milestones appropriately and perform better than those exposed to valproate, but studies investigating development beyond the pre-school years are more limited across certain neurodevelopmental areas in comparison to unexposed children. Additionally, data from children exposed to higher doses of these two medications are also more limited. Despite evidence regarding an increased risk of reduced fetal growth and increased risk of cleft anomalies, there is a lack of conclusive data regarding topiramate exposure and child neurodevelopmental outcome. Data are even fewer for other antiseizure medications and absent for others, which undermines preconceptual care for women with epilepsy. Methods of data collection in this context and aims for an improved focus on these outcomes are discussed.

## Next steps- candidates for surgery in MRI-negative epilepsy

**Fernando Cendes, MD, PhD, FAAN**

*Department of Neurology, University of Campinas, UNICAMP, Brazil.*

Imaging is pivotal in the presurgical evaluation of patients with pharmaco-resistant epilepsies. High-resolution structural neuroimaging with magnetic resonance imaging (MRI) plays a vital role in defining the etiology, epilepsy syndrome, and surgical prognosis. It is essential that structural MRIs are optimally acquired, including 3D T1-weighted and FLAIR sequences, and carefully reviewed by trained experts within the context of all available clinical and EEG data. Multiplanar reformatting of high-resolution MRI and correlation with functional multimodal imaging improves the detection of subtle lesions. Detection of a lesion on a previous negative MRI has a substantial impact on determining the etiology of epilepsy, reducing the need for invasive investigations, and planning surgical treatment in patients with pharmaco-resistant seizures and for the postoperative outcome. The high diagnostic yield of MRI to identify the common pathological findings in individuals with focal seizures, including mesial temporal sclerosis, vascular anomalies, low-grade glial neoplasms, and malformations of cortical development (MCD), has been well established. Quantitative postprocessing may help to complement the evaluation of subtle MCDs. Positron emission tomography (PET) is the most performed interictal functional neuroimaging technique that may reveal a focal hypometabolic region concordant with seizure onset. Single-photon emission computed tomography (SPECT) studies may assist the performance of ictal neuroimaging in patients with pharmaco-resistant focal epilepsy. Emerging advanced postprocessing of functional imaging modalities, such as functional MRI (fMRI), and EEG-fMRI, may help to reduce the need for invasive investigations and predict prognosis.

## Management of epilepsy caused by focal cortical dysplasia

**Saeid Charsouei,MD**

*Assistant Professor of Neurology, Fellowship in Epilepsy, Tabriz University of Medical Sciences.*

The incidence of Focal Cortical Dysplasia (FCD) is almost 50% of all the cases of intractable epilepsy identified in adults and children. Antiepileptic drugs (AEDs) have been widely used in the treatment of FCD. However, evidence to suggest their specific effect in the treatment of FCD remains to be established. Although treatment currently involves surgical management, noninvasive treatments have been identified. non-invasive management strategies including, 1-mammalian target of rapamycin (MTOR)inhibitors, 2- ketogenic diet (KD), and 3- vagus nerve stimulation (VNS). Commonly used drugs in the treatment of drug-resistant epilepsy are broad spectrum AEDs such as levetiracetam, topiramate, and zonisamide for their multiple mechanisms of action. Epileptic seizures in focal cortical dysplasia are difficult to control with pharmacological treatment and often intractable. Hence, the surgical treatment appears to be a next therapeutic procedure. The resection of lesion, lobectomies and even hemispherectomies are performed. More limited surgeries are performed in elderly patients, usually due to FCD type I, usually located within the temporal lobe. Younger patients usually have FCD type II, with more extensive lesions and extratemporal location, predominantly in the frontal areas. In these cases operation includes lobectomy/ies or even hemispherectomy. According to the literature, 60–80% of patients remain seizure-free after surgery, depending on the study center.

## Diffusion MRI in drug-resistant epilepsy

**Luis Concha**

*Associate Professor, Institute of Neurobiology, National Autonomous University of Mexico, Mexico.*

Analysis of diffusion-weighted MRI (dMRI) allows for non-invasive inference of tissue microstructure. Through mathematical models and representations, it is possible to obtain information at the microscopic level. In the last two decades, dMRI has become a valuable research tool in many fields of neurology, including epilepsy, where it has been used to document extensive brain abnormalities in patients with various forms of epilepsy. Slowly but surely, it has also proven to be a valuable tool for the diagnostic workup of drug-resistant epilepsy patients, aiding in the detection of epileptogenic lesions and associated abnormalities of brain connectivity. Finally, it has shown tremendous potential to aid in the prediction of seizure freedom following surgical resection, as well as post-surgical alterations of cognitive performance. In this talk I will briefly discuss the biophysical underpinnings of dMRI and example applications, with special emphasis on the realistic extent of the technique for accurate clinical interpretation.

## Utility of FDG PET/CT scan in seizure focus localization in patients with non-lesion brain MRI

**Abtin Doroudinia<sup>1\*</sup>, Mehrdad Bakhshayesh Karam MD, Jafar Mehvari MD, Sohrab Fesharaki MD**

*<sup>1\*</sup>National Research Institute of Tuberculosis and lung diseases (NRITLD), Masih Daneshvari Hospital, Tehran, Iran.*

Brain MRI fails to reveal apparent abnormality in approximately 20% of patients with medically refractory epilepsy. FDG PET/CT is highly sensitive in localizing epileptogenic foci and is able to provide information complementary to MRI imaging. This is a cohort study aiming to evaluate patients suffering from refractory epilepsy and unremarkable MRI. We stratified patients with regard to clinical epileptogenic focus as localized in temporal lobe, frontal lobe or partially localized and tried to find out in which group of patients PET/CT is most congruent with clinical and EEG findings.

In this study we included 99 patients. 63 patients had their seizure focus localized in temporal lobe by means of clinical and EEG evaluation in which 32 of them demonstrated exactly congruent PET/CT results (50.8%). Remainder of these patients demonstrated either partially congruent PET/CT results (7 patients, 11.1%) or totally incongruent PET/CT findings (24 patients, 38.1%). 24 patients had their seizure focus localized in frontal lobe by means of clinical and EEG evaluation in which only 3 (12.5%) of them demonstrated partial congruency with PET/CT results. The remainder of 21 (87.5%) patients demonstrated incongruent PET/CT results and there was no case in frontal lobe focal seizures with congruent PET/CT results. 12 patients had their seizure focus only partially localized in one hemisphere in which 6 (50%) patients demonstrated partial congruency with PET/CT results.

FDG PET/CT is useful tool to evaluate patients with refractory seizure who had localized seizure in temporal lobe on clinical evaluation. Utility of FDG PET/CT scan in extratemporal seizure foci is much more limited. Our results need to be further validated in larger studies.

## Neuroimaging in focal epilepsy

**John S Duncan**

*National Hospital for Neurology and Neurosurgery, Queen Square, London, UK.*

Epilepsy is the most common serious neurological disorders. Neuroimaging is important for diagnosis and for guiding treatment. X-ray CT is important acutely, for clarifying calcification, and if MRI is contra-indicated.

MRI identifies major pathologies underlying focal epilepsies. Epilepsy MRI protocols, 3T MRI and review with skilled neuro-radiologists increases the yield. 7T MRI has increased sensitivity, but also generates more artefacts than 3T MRI. Quantitative and computational analysis of MRI may identify abnormalities that are not evident visually. Analysis of grey and white matter identifies cerebral atrophy and abnormalities of white matter.

High resolution MRI is important to select patients for epilepsy surgery and 3-dimensional multimodal imaging aids interpretation and decision making. Functional MRI and tractography map eloquent cortex and critical white matter tracts, so these may be identified and used to modify the surgical approach to minimise the risk of surgical morbidity.

If MRI is unremarkable, FDG-PET may help to identify the region of an epileptic focus, as may ictal SPECT, and neurophysiological imaging with electrical and magnetic source imaging. Specific PET ligands that bind to GABA<sub>A</sub>, opioid and NMDA receptors give information on the pathophysiology of epilepsy, and may be useful biomarkers for assessing disease-modifying therapies.

## Future aspects of using outpatient long-term monitoring

**Jonas Duun-Henriksen**

*Head of Epilepsy Science, UNEEG medical, Lyngø, Denmark.*

It is well established, that often, clinicians are left with inaccurate seizure occurrence information from diaries or intermittent in-hospital EEG registrations when making epilepsy management decisions. Wearables and ultra long-term subcutaneous EEG monitors are starting to surface and show valuable objective seizure information to guide treatment based on the everyday life of people with epilepsy. Adoption of subcutaneous, ultra long-term EEG monitoring may cause a shift from subjective seizure reporting to objective seizure counting but can also aid in utilizing seizure cycles, sleep and IED in the optimization of therapy.



## Management of Post-Traumatic Seizures and Epilepsy

**Majid Ghaffarpour, MD**

*Professor of Neurology, Tehran University of Medical Sciences.*

Traumatic brain injury (TBI) is the third most common cause of epilepsies and post-traumatic epilepsy accounts for 4% of all epileptic patients. Over 2% of patients attend to emergency departments in UK each year with head trauma. In USA more than 3 billion people suffer a TBI with approximately 300.000 hospitalizations, 50.000 mortality, and 56.3 billion annual costs. TBI causes both primary and secondary injuries to the brain. Secondary injuries include inflammation, neurodegeneration, post transitional modifications (PTMs) following protein synthesis, mossy fibers sprouting, astrocytes activation and neuronal synchronization, leading to not only post traumatic epilepsy (PTE) but also psychiatric disorders such as anxiety, post-traumatic stress disorder (PTSD) and behavioral disorders as well as neurological disturbances including dementia. Brain injury leads to different types of seizures, treatment of which requires specific attention to their risk rates for developing epilepsy. In this lecture in addition to management of post traumatic seizures and epilepsy, important related issues including risk factors for developing PTE and new prophylactic therapies, targeting cytokines, inflammation mediators, astrocytes and other factors involved in neurodegenerative processes, e.g., ISO1 (macrophage migration inhibitory factor antagonist), apocynin (NADPH-oxidase inhibitor) minozac (selective inhibitor of proinflammatory cytokine activated glia), rapamycin (mTOR inhibitor) and trametinib (highly specific and potent MEK 1/2 inhibitor) will be discussed.

## How to diagnose and treat post-stroke seizure and epilepsy

**Kurosh Gharagozli, MD**

*Professor of Neurology, Shahid Beheshti University of Medical Sciences.*

Post-stroke epilepsy (PSE) is an important event after cerebrovascular accidents, treatment options are still limited. While many physicians prescribe antiepileptic drugs (AED) for secondary prevention of PSE, it is unclear which drug is the most effective in control of recurrence of seizures.

PSE is divided into early and late seizures. Early seizures occur within the first week after stroke. This is also termed 'acute symptomatic seizures', Late seizures have a peak incidence of 6-12 months after stroke.

There are some consequences after stroke that are etiologies of PSE, including: hypoxia, metabolic dysfunction, global hypoperfusion, hyperperfusion, glutamate excitotoxicity, ion channel dysfunction and BBB disruption in the acute phase. Above factors leading to early seizure.

Gliotic scarring, chronic inflammation, angiogenesis, neurodegeneration, neurogenesis, axonal and synaptic sprouting, selective neuronal loss, and altered synaptic plasticity are main suspects as mechanisms of late seizures. Glutamate has been also known to produce epileptiform discharges in surviving neurons. For control and treatment of PSE we should know about the type of PSE. For primary prevention: In clinical studies, LEV was associated with improved outcomes after intracerebral hemorrhage. Aspirin and statins have been reported to have a role in preventing epileptogenesis and may also be effective for PSE.

For Secondary prevention it is uncertain which AED are the most effective for the prevention of recurrence of seizure. According to ILAE report CBZ, LEV, PHT, zonisamide (ZNS) are approved as an initial monotherapy in adults with PSE.

Second generation drugs may be considered because of the lower incidence of side effects and interactions.

In conclusion Physicians should always treat stroke survivors with the risk of PSE in mind.

Future studies analysis may also be useful in predicting who will develop PSE.

## **Surgical Management of MR-Negative Epilepsy**

Walter J Hader

Division of Pediatric Neurosurgery, Department of Clinical Neurosciences, Alberta Children's Hospital, Calgary, University of Calgary, Alberta, Canada.

Surgical management of patients with refractory epilepsy in the context of normal MR imaging is an increasingly more common and challenging scenario presenting to epilepsy surgery centres. Historical seizure freedom rates after surgical intervention, however, were modest with the odds of seizure freedom remaining significantly higher in the presence of a lesion on MR. As a result, many patients with normal MR imaging may not have even been considered for an initial surgical evaluation. Upon completion of comprehensive presurgical investigations, patients ultimately considered candidates, uniformly require the additional step of intracranial EEG, often in the form of extensive subdural implantation to adequately define the Seizure Onset Zone (SOZ) and determine surgical candidacy. Recent reports of Stereotactic EEG (SEEG) for intracranial investigations has now demonstrated that it is the safest, best tolerated and most effective method of intracranial implantations in defining the SOZ in patients with normal MR imaging. Seizure freedom may be possible in over half of properly selected patients with normal MR imaging after SEEG guided treatments, approaching the outcome of lesional epilepsy patients subjected to similar intracranial EEG evaluations.

## Extensive malformation of cortical development

**Samaneh Haghghi, MD**

*Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran.*

Malformations of cortical development (MCDs) are a spectrum of rare disorders causing developmental delay and epilepsy. Extent of malformation and underlying genetic characteristics of MCDs determine the severity of manifesting feature of disorders. MCDs caused by disruption of three fundamental stages of corticogenesis: cell proliferation, neuronal migration and post-migrational development. Although definite diagnosis of MCDs is based on pathology of tissues, neuroimaging plays an important role in diagnosis and classification of MCDs due to unavailability of tissue pathology. With improved genetic methodologies, the underlying molecular and pathological features of several MCDs have been recently clarified. The purpose of this Review is to provide standard MCDs terminology and classification according to disturbed stage of corticogenesis, some genetic mutation and common radiological features of them.

## Pharmacotherapy for Nonconvulsive Status Epilepticus

**Lawrence J. Hirsch, MD**

*Comprehensive Epilepsy Center, Department of Neurology, Yale University School of Medicine, New Haven, USA.*

Nonconvulsive status epilepticus (NCSE, which includes electrographic SE) is defined as 10 or more continuous minutes of nonconvulsive seizure activity; or nonconvulsive seizures adding up to  $\geq 20\%$  of any hour of recording (ACNS terminology, 2021). Nonconvulsive seizures/NCSE are common, especially in patients with coma or prior seizures. The chances of neurological decline and other adverse long term outcomes increase at higher seizure burdens, as has been shown in all ages and in many different clinical scenarios. There are no prospective randomized trials on treatment of NCSE, so most treatment is extrapolated from literature on convulsive SE. Thus, IV levetiracetam, valproate and fosphenytoin are first line medications. There is one class I prospective randomized trial on treatment of refractory nonconvulsive seizures (not SE): the TRENdS trial, which showed that lacosamide was non-inferior to fosphenytoin; it was actually non-significantly more effective with equal tolerability. In addition to those options, IV brivaracetam is a reasonable option, and add-on enteral medications can be helpful. General principles are that diagnosis should be as early as possible (consider use of rapid EEG devices/caps); dosing can start lower than in convulsive SE, but with close follow-up and additional doses as needed; seizure burden matters; and stop medications if there was no hint of efficacy with a full load. Other than after convulsive seizures/CSE, we try to avoid using coma-inducing medication for nonconvulsive seizures/NCSE, though it is sometimes necessary. The Yale protocol will be presented as well.

## The quality of life in patients of epilepsy

**Mehran Homam, MD**

*Associate professor of neurology*

*Department of neurology, Mashhad Branch, Islamic Azad University, Mashhad, Iran.*

Epilepsy is a chronic disorder with enormous psychological and social consequences. It might affect patients in different age groups and also in different epileptic syndromes.

Research on the title of quality of life in epilepsy is defined by a wide range of methodology, including both in terms of study design and instruments has been designed. in the general population Quality of life is better than in patients with epilepsy; it might be worse in patients with epilepsy than that in patients with other chronic conditions; and it might be similar to that of healthy persons if patients with epilepsy be well-controlled. one of the most relevant determinants of poor quality-of-life (QOL) scores is frequency of seizures, and co-existence of depression could worsen quality of life.

The impact of surgical treatment affects the quality of life in epileptic patients, in all ages, in correlation with seizure control. The role of antiepileptic drugs is controversial. the most investigated domains of quality of life in epilepsy are in emotional status and cognition.

It is clear that in many researches the evaluation of quality of life and psychosocial functioning in people with epilepsy have been showed. however, the lack of a standardized approach results in difficult conclusion. Still there is no unique platform to know what measures should be used, in which patients, and in which sub-populations. With further sensitive measures of quality of life, it seems no longer appropriate to consider seizure frequency alone.

## Seizure Imitators in Pediatric Patients

**Mohsen Javadzadeh,MD**

*Pediatric Neurologist, Pediatric Clinical Neurophysiologist, Mofid Children Hospital, Shahid Beheshti University of Medical Sciences.*

The terminology on the topic has been variable and confusing. Seizure is from to the verb: seize but may mean different meanings to different people, such as any type of spell, or epileptic seizure.

PNES means psychogenic nonepileptic seizure, and it is in contrast with another term: Paroxysmal (both Physiologic and Psychologic) nonepileptic seizure. Strictly speaking, terms like nonepileptic seizures, nonepileptic spells, and nonepileptic events include any episode that mimics epileptic seizures. Paroxysmal Physiologic NonEpileptic Seizures: Neonates, Infants, Toddlers include: Jitteriness, Benign Myoclonus, Head Banging, Body Rocking, Startle Disease or Hyperekplexia, Cyanotic Breath-Holding Spells, Self Gratification, Shudderings, and Paroxysmal Vertigo.

In Children we face other condition such as: Night Terrors (Pavor Nocturnus) and Nightmares, Sleep walking (Somnambulism) and sleep talking (Somniloquy), Tics, Chorea, Staring Spells (Daydreaming), Stereotypic Movements, Rage Attacks (Episodic Dyscontrol Syndrome) Munchausen Syndrome by Proxy, and Recurrent Abdominal Pain and in the adolescents still other conditions are more common. Some of them are as follows: Syncope, Narcolepsy and Cataplexy, Basilar Migraine, Confusional Migraine, Tremor, and Panic Disorders.

PNESs, as the focus of this discussion, resemble epileptic seizures and present as a sudden, involuntary, time-limited alteration in behavior, motor activity, autonomic function, consciousness, or sensation. However, unlike epilepsy, PNESs do not result from epileptogenic pathology and are not accompanied by an epileptiform electrographic ictal pattern. PNESs comprise 30% of all paroxysmal nonepileptic events in children.

Unfortunately, once the diagnosis of “seizures” is made, it is easily perpetuated without being questioned and is difficult to undo, which explains the usual diagnostic delay in differentiating non-seizure and non-epileptic events from true epileptic seizures. One of the key clues to think about seizure-mimickers in the first step could be resistance to many antiepileptic drugs.

In this brief review, different conditions in children that may mimic epileptic seizures will be discussed and illustrated better with showing video clips of them.

## Valproate in the treatment of epilepsy and status epilepticus

**Hossein Kahnouji MD**

*Neurologist, Epilepsy fellowship.*

Antiepileptic property of valproate was discovered in 1962, when it was tested as a solvent for other molecules being checked for anticonvulsant activity. It has the broadest spectrum of anticonvulsant action compared to all currently available antiepileptic drugs (AEDs), both in adults and children. It has epigenetic effect in several fields specially cancer treatment. Pharmacodynamics of valproate: enhances GABA synthesis and release, reduces the release of the excitatory molecules (NMDA) and blockade of voltage gated ionic channels.

Valproate is effective against all the types of seizure and epileptic syndromes, both in pediatric and adult patients. In particular, it has been tested in both generalized (tonic-clonic, absences and myoclonic) and focal seizures, and it has been found effective in Lennox-Gastaut, West and Dravet syndrome.

The efficacy, safety and tolerability of intravenous (IV) valproate has also been evaluated in the management of generalized convulsive status epilepticus. Valproate has supra additive effect in some combination of antiseizure medicines.



## Important biophysical and technological aspects of EEG for clinical applications

**Hossein Kahnouji MD**

*Neurologist, Epilepsy fellowship.*

The EEG is an electrophysiological technique for the recording of electrical activity arising from the human brain. EEG is the most commonly used functional investigative method in epilepsy.

For the first time Hans Berger, a German psychiatrist, recorded electrical activity of human brain. He described the human alpha and beta rhythms and published his paper in 1929. finally, in 1980 digital EEG system was introduced.

In this lecture I explain how EEG signals are generated in the brain and how they are recorded by the EEG machine. Also, I explain a number of Electrical Circuit elements and important components of EEG machine such as electrodes, filters, amplifier, analog to digital convertor.

Understanding these basics is essential for interpretation of clinical EEG.

## **Nonconvulsive status epilepticus: etiology, clinical features and prognosis**

**Peter W. Kaplan**

*Department of Neurology, Johns Hopkins University School of Medicine, Johns Hopkins Bayview Medical Center, Baltimore, Maryland, USA.*

The clinical features of non-convulsive status epilepticus (NCSE) can vary from minimal and highly subtle, to coma. A classification of NCSE is presented which includes genetic types of typical absence status, non genetic atypical NCSE as seen in Lennox-Gastaut Syndrome, and the rarer types of generalized status epilepticus. The clinical features of localization related status epilepticus may vary from sensory, motor, autonomic with or without perturbation of vigilance and consciousness, and other rarer features which will be presented descriptively and in tabular form. I discuss approaches to diagnosis, management and treatment, as well as prognosis.

## Closed-loop systems for Epilepsy

**Esther Krook-Magnuson, PhD**

*Associate Professor, Department of Neuroscience, University of Minnesota, Minneapolis, MN, USA.*

Closed-loop approaches come in a variety of forms; on-demand responsive intervention strategies are one example of a closed-loop approach. Through online seizure detection, on-demand intervention provides temporal specificity. On-demand optogenetic intervention provides additional cell-type, spatial, and direction of modulation specificity. Such a highly selective intervention strategy can be a successful strategy, as illustrated by selective on-demand optogenetic inhibition of dentate gyrus granule cells near the seizure focus. On-demand optogenetic interventions can also be used to gain deeper insight into the epilepsies, and to explore potential intervention targets distant from the seizure focus, as illustrated by on-demand optogenetic work targeting the cerebellum. This work additionally illustrates that specificity of intervention can also be critical to providing robust seizure inhibition. While optogenetics is an excellent research tool, it is not yet clinically available to epilepsy patients. Electrical stimulation provides an opportunity for more immediate translation, but deciding on appropriate stimulation parameters (e.g., frequency, pulse width, amplitude) can be critically important to success. Bayesian optimization with Gaussian process regression is an additional example of a closed-loop approach, and can be coupled with on-demand intervention strategies. Using this approach, we demonstrate robust inhibition of hippocampal seizures in a mouse model of temporal lobe epilepsy via on-demand electrical stimulation of the cerebellum. Closed-loop optimization approaches have the potential to aid in the clinical realization of successful stimulation interventions.

## The genetics of pharmacoresistance in mesial temporal lobe epilepsy

**Iscia Lopes-Cendes, M.D., Ph.D.**

*Professor of Medical Genetics and Genomic Medicine*

*Head, Laboratory of Molecular Genetics*

*Department of Translational Medicine, School of Medical Sciences, University of Campinas  
(UNICAMP), Campinas, Brazil.*

Mesial temporal lobe epilepsy (MTLE) is the most common type of focal epilepsy in adults. Many anti-seizure medications (ASMs) are available for treating patients with epilepsy. However, even with optimal clinical treatment, at least one-third of patients with MTLE will be pharmacoresistant. Pharmacoresistance to ASM is likely a multifactorial condition involving genetic and environmental factors. In recent years, the increased knowledge generated by genetic discoveries provided powerful tools to study the contribution of genetics to disease and response to treatment in many disorders. The genetic aspects influencing pharmacoresistance to ASMs are thought to affect the classic mechanisms in pharmacology, such as pharmacokinetics and pharmacodynamics. In this lecture, I will present and discuss the contribution of genetic factors to understanding the basic mechanisms determining pharmacoresistance in patients with MTLE. Furthermore, I intend to provide an overview and a critical discussion of the findings, limitations, new approaches, and future directions of these studies aiming to improve the treatment of patients with pharmacoresistant MTLE.

## Optimizing Status Epilepticus management during the COVID-19 pandemic

**Dr. Asieh Mehramiri**

*Department of neurology, Faculty of medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran*

Status Epilepticus (SE) can represent a neurological manifestation of SARS-CoV-2 infection. It can occur before respiratory or systemic involvement of COVID-19, although more frequently it occurs within the context of a clinically overt respiratory infection. The lack of prompt access to EEG recordings may lead to an underestimate of its incidence, particularly for Non-Convulsive Status Epilepticus.

The etiology of SARS-CoV-2-related SE remains mostly unknown. A direct role of SARS-CoV-2 invasion in the CNS or the systemic inflammatory syndrome due to cytokine release has been proposed as possible explanations. However, the association between SE and COVID-19 could be spurious, and there may be other underlying conditions causally and independently related to both SE and COVID-19.

In treating SE, physicians will be challenged by the need for ICU resources and ventilators in the era of the COVID-19 pandemic. The optimal approach could be minimizing anesthesia and intensive care unit (ICU) admissions for SE, with proper exclusion of psychogenic nonepileptic status and consideration ASD-antiviral medication interactions. A multidisciplinary approach are required that will use creative solutions, non-sedating ASDs, and risk–benefit calculations to best management of SE in this resource-constrained time.

## The epidemiology of Nonconvulsive Status Epilepticus

**Boulenouar Mesraoua, MD, FAAN**

*Associate Professor of Neurology, Hamad Hospital and Weill Cornell Medical College, Qatar.*

Prolonged nonconvulsive seizures have been described at least since the 19th century, although their recognition in the Status Epilepticus category was not made until 1962. Since then, several epidemiological studies of NCSE have been undertaken, with different results ; It is difficult to accurately estimate the prevalence of NCSE; the prevalence of NCSE depends on the definition used; two recent interesting dates in the history of the NCSE have opened a new era for NCSE epidemiological studies; in 2013, following an extensive review of abnormal EEG epileptiform discharges ,the Salzburg Consensus Statement proposed working diagnostic criteria for NCSE and highlighted the use of unified EEG terminology.

Additionally, in 2015, the International League Against Epilepsy highlighted the importance of operational timelines for the early detection and treatment of status epilepticus, particularly NCSE.

Recognition of NCSE can be particularly challenging, as a wide range of differential diagnoses in different populations must be considered.

This presentation will highlight the evolution of epidemiological research regarding NCSE before and after the periods 2013-2015

## Updates on Treatment Strategies in Pediatric Epilepsy

**Mahmoud Mohammadi MD**

*Professor, Pediatric Neurology  
Head, Epilepsy Monitoring Unit  
Children's Medical Center, Tehran University of Medical Sciences.*

Epilepsy is an umbrella term for a common neurological disorder in children, affecting more than 5 cases in every 1000 of general pediatric population. Intractability or refractoriness in about 30% of the affected population has led to overwhelming growth in the pharmacologic armamentarium as well as non-pharmacologic treatments of epilepsy in the last century and especially in the recent decades.

Tremendous progress in basic sciences especially in “genetics” has changed the “treatment paradigms” in pediatric Epileptology from more simple semiological and syndromic approach to targeted approach (i.e. precision medicine) to epilepsy treatment. Nowadays rather than dealing with a single entity such as “Ohtahara syndrome”, we are confronting a wide spectrum of “Early Infantile Epileptic Encephalopathy, EIEEs” with different genetic mutations and a variety of genes involved, each of them seeks different treatments based on the end-point product (protein) of that gene, resulting different functions of that protein. Some of them per se are responsive to sodium channel blockers while others are quite resistant to it. This different new paradigm is the basis for targeted approach to epilepsy treatment in children.

On the other hand many recent advances in pediatric epilepsy surgery has improved the outcome and decreased morbidity in comparison to previous conventional methods. Different technics of ablation of the epileptogenic zone such as thermal and ultrasonic ablations have replaced old resective operations.

Updates and improvements in ketogenic diet have also changed the practicality and palatability of this treatment method and in addition to reduction in side effects has increased the success rate of this method. Ketogenic diet is also an efficient method and a good alternative to epilepsy surgery in countries with “low income” economies.

## ILAE clinical practice recommendations for the medical treatment of depression in adults with epilepsy

**Marco Mula MD PhD FRCP FEAN**

*Atkinson Morley Regional Neuroscience Centre, St George's University Hospital and Institute of Medical and Biomedical Education, St George's University of London, London, United Kingdom.*

Depression represents one of the most frequently encountered comorbidities among adults with epilepsy affecting 1 in 4 individuals. During the last few years, the ILAE worked on the development of clinical practice recommendations for the treatment of depression in adults with epilepsy. The working group consisted in members of the Task Force of the ILAE Commission on Psychiatry, ILAE Executive and IBE representatives. The development of these recommendations is based on a systematic review of studies on the treatment of depression in adults with epilepsy, and a formal adaptation process of existing guidelines and recommendations of treatment of depression outside epilepsy using the ADAPTE process.

The document focuses on first line drug treatment, inadequate response to first line antidepressant treatment, duration of such treatment and augmentation strategies, within the broader context of electroconvulsive therapy, psychological and other treatments. For mild depressive episodes, psychological interventions are first line treatments and where medication is used, Selective Serotonin Reuptake Inhibitors (SSRIs) are first-choice medications (Level B). SSRIs remain the first choice medications (Level B) for moderate to severe depressive episodes, however, in patients partially or non-responding to first line treatment switching to venlafaxine appears legitimate (Level C). Antidepressant treatment should be maintained for at least 6 months following remission from a first depressive episode but it should be prolonged to 9 months in patients with a history of previous episodes and should continue even longer in severe depression or in cases of residual symptomatology until such symptoms have subsided.



## Antiseizure medication exposure in infants of breastfeeding mothers with epilepsy

Syed Navid Naghibi, MD

*Neurologist, Fellowship of Epilepsy at Isfahan University of medical science.*

Several studies have demonstrated that breastfeeding is safe for children of mothers who are taking an ASM. Breastfeeding has many short-term and long-term health benefits for mothers as well as for infant health, immunity, growth, and development. In the general population, the benefits of breastfeeding are widely documented and include nutritional benefits, protection against common childhood infections, and improved survival during the 1st year, including a lower risk of Sudden Infant Death Syndrome. Thus, the American Academy of Pediatrics strongly advocates for breastfeeding and recommends exclusive breastfeeding of infants for the first 6 months of life and continued breastfeeding for a year or longer with complementary food.

Despite known health benefits, breastfeeding in women with epilepsy (WWE) face unique challenges: Breastfeeding safety in WWE has been debated for many years because of the scarcity of data on the degree of antiseizure medication (ASM) expression in breastmilk and short-and long-term infant health and developmental effects of ASM exposure related to breastfeeding. Exposure to ASMs via breastmilk and the lack of clear guidelines for breastfeeding recommendations in WWE lead to variable practices in breastfeeding education, and as well as dissuasion by some clinicians, due to safety concerns. Two studies in WWE showed no increased risk for poor cognitive outcomes at 3 years old and one study showed improved verbal outcomes at age 6 years old in infants that were breastfed.

It is important to counsel postpartum women that the benefits of breastfeeding outweigh the risks; however, certain precautions should be kept in mind. Awakening several times at night in order to feed the baby will cause sleep disruption that could lead to increased seizure frequency. We encourage family and friends to help with nighttime feedings so that the mother can get an uninterrupted 6–8 h of sleep.

## Advances in pharmacotherapy of sleep-related epilepsy

**Mohammad Reza Najafi, MD**

*Professor of Neurology, Isfahan University of Medical Sciences.*

Sleep-related epilepsy represents nocturnal seizures that manifest solely during the sleep state. Approximately 12% epileptic patients are affected by sleep related epilepsy with the majority suffering from focal epilepsy.

Treatment of sleep-related epilepsy should take in account the type of epileptic syndrome, the type of seizures, the patient characteristics, and also the pharmacokinetics of the drug. Proper characterization of the epilepsy is essential to choose appropriate antiepileptic drugs. Drugs effective in focal epilepsy may be used to treat benign genetic focal epilepsies such as rolandic epilepsy and other focal (frontal or not) sleep epilepsies. These include both classical (such as carbamazepine) and new (such as levetiracetam and lacosamide) antiepileptic drugs. Drug-resistant cases should be evaluated for epilepsy surgery, which may be efficacious in this setting. Valproate, lamotrigine, topiramate, levetiracetam, and perampanel are effective. Specific syndromes such as ESES require specific treatment such as a combination of high dose steroids, benzodiazepines, levetiracetam, and even surgery when an epileptogenic lesion is present. Sleep disorders that may worsen epilepsy such as obstructive sleep apnea or insomnia should be adequately treated to improve seizure frequency. Adequate control of seizures during sleep decreases risk of SUDEP.

The purpose of this review is to summarize and discuss current options and new advances in the treatment of sleep-related hypermotor epilepsy (SHE), Childhood epilepsy with centro temporal spikes (CECTS), and Panayiotopoulos Syndrome (PS) are three of the most frequently implicated epilepsies occurring during the sleep state.

## Management of epilepsy caused by nodular heterotopia

**Mahyar Noorbakhsh, MD**

*Epileptologist, Kashan university of medical sciences, Kashan, Iran.*

Malformations of cortical development (MCDs) are a heterogeneous group of inherited disorders of disrupted cerebral cortex formation caused by various etiologies such as genetic, vascular or metabolic.

Grey matter heterotopia are disorders caused by abnormal neuronal migration and consists of normal neurons in abnormal locations. These disorders are nodular or linear formation and are in the periventricular or subcortical location. Periventricular nodular heterotopia (PVNH) is the most common type and manifested by drug resistant epilepsy and intellectual disability and others.

The nodular heterotopia usually manifested with drug resistant epilepsy and treatment often has many challenging issues. the most problem point is the connectivity between heterotopic nodules and adjacent cortex and other near structures such as hippocampus. The best management need to define this network accurately and planning a correct strategy for access to this network.

Treatment options for this disorder varies and consists of surgical process such as temporal lobectomy or lesionectomy. According to the previous experiences, due to the deep-seated location, PNH are seldom accessible surgically without facing a high potential of neurological deficits and lesionectomy is mostly limited to cases with unilateral and single nodule with proper surgical accessibility.

Two main stereotactic ablative treatments are SEEG-guided radiofrequency thermocoagulation (RFTC) and MRI-guided laser interstitial thermal therapy (MRG-LITT). Although, the experiences about these procedures are limited and is based on case reports and series but the date is growing. these procedures due to little adverse effects and focused intervention may become the best treatment in the future.

## Antiepileptogenesis and disease modifying therapy

**Terence J. O'Brien**

*Department of Neuroscience, CCS, Monash University. The Department of Neurology, Alfred Health, Melbourne, Australia.*

Epilepsy the most common, serious chronic neurological disease worldwide, affecting >50 million people globally. Despite many new anti-seizure medications drugs (ASMs) being introduced into practice over the past 20 years, the treatment outcomes remain unsatisfactory for many patients. Current treatment with ASMs is symptomatic, suppressing seizures but not having sustained effects, and no effects on the accompanying comorbidities. There has been little reduction in the proportion of patients who are refractory to medical treatment, with approximately one third continuing to have seizures despite trials of treatment with multiple different AEDs. There is no medical treatment that has been demonstrated to be effective at preventing the development of epilepsy after an epileptogenic insult, to prevent progression of the epilepsy or its comorbidities, or to mitigate or cure the condition. A major challenge for translational researchers is to discover and develop new treatments that address these major treatment gaps, in particular to develop treatments that can prevent or mitigate the development of epilepsy (i.e. anti-epileptogenic), mitigate its severity (including ASM resistance), or even cure the epilepsy. Advances in the understanding of the fundamental neurobiology of seizures and epileptogenesis have suggested new targeted approaches by which this may be achieved. Rigorous evaluation of these with studies using clinically relevant “true epilepsy” models is essential to provide the evidence base to select the most promising novel treatments to translate into clinical trials, and then to ultimately improve outcomes for patients with this disabling condition.

## The global burden and care of epilepsy in Iran

**Hossein Pakdaman, MD**

*Professor of Neurology, Shahid Beheshti University of Medical Sciences.*

Epilepsy has garnered increased public health focus because patients who suffer from epilepsy experience pronounced and persistent health and socioeconomic disparities despite treatment and care advances. The epidemiology of epilepsy is diverse in different countries and regions.

This nationwide population-based cross-sectional study was conducted to determine the life time prevalence and health related factors of epilepsy for the first time in Iran through a two-phase door- to-door survey method. In phase I, a screening for epilepsy was performed on 68,035 people. Then in phase II, after the neurological evaluation of participants and reviewing medical records, 1130 subjects with epilepsy was confirmed. The life time prevalence of epilepsy was achieved to be 16.6 per 1000 people (95% CI 15.4–17.8) with the average age onset  $19.1 \pm 21.1$  (active prevalence 9.5 per 1000 people). Focal seizure (59.3%), generalized epilepsy (38%) and unknown types of epilepsy (2.7%) were detected among participants. The overall life time prevalence of febrile convulsion was 4.1 per 1000 people. The frequency of attacks per year and per month were  $3.0 \pm 1.6$  and  $0.5 \pm 0.1$ , respectively. Age-specific life time prevalence was highest among the age group of 15–19 years old [32.7 per 1000 persons (95% CI 29.1–36.8)] and it was higher in male (53.8%) than female (46.2%) participants. Our results showed that the life time prevalence of epilepsy in Iran is higher than worldwide.

## Classification of seizures and the epilepsies in neonate

**Ronit M Pressler PhD MD MRCPCH**

*Consultant in Clinical Neurophysiology, Great Ormond Street Hospital for Children,  
Associate Professor in Clinical Neuroscience, UCL Great Ormond Street Institute of Child Health,  
London, UK.*

Seizures are the most common neurological emergency in the neonatal period and are associated with mortality and long-term neuro-disability. The clinical diagnosis is challenging because most have no or only discreet clinical manifestation. Depending on the aetiology, up to 60% of seizures are electrographic only. Critically ill infants with a very high seizure burden or in status epilepticus are particularly likely to lack clinical manifestation. Thus, clinical diagnosis is unreliable in most cases making EEG diagnosis a necessity. This makes the integration into a classification serving all ages difficult. Recently the ILAE has published a position paper outlining a new classification for neonatal seizures to provide neonatologists, paediatricians and neurologists a common language to identify, diagnose, and treat neonatal seizures and their acute aetiologies. This classification uses the same framework and terminology as the 2017 ILAE seizure classification, but is tailored towards neonates. All neonatal seizures are considered of focal onset and should be confirmed electrographically. Seizures types include motor events (automatisms, clonic, epileptic spasms, myoclonic, sequential, tonic) or non-motor events (autonomic, behavior arrest) or be electro-graphic only. It allows the user to choose the degree of detail when classifying seizures while takes underlying pathophysiological mechanism into account. A further position paper is in proposed defining and outlining epilepsy syndromes with onset in the neonatal period and infancy.

## Neuroimaging of Psychogenic Nonepileptic Seizures

**Markus Reuber**

*Academic Neurology Unit, University of Sheffield, Royal Hallamshire Hospital, Sheffield, UK.*

Although as many as one in five patients presenting to neurologists with blackouts or seizures has Psychogenic Nonepileptic Seizures (PNES, also labelled dissociative or functional seizures), and despite the fact that PNES disorders cluster into a discrete number of stereotyped sets of experiences and behaviours, our understanding of the pathophysiology is still limited. Whereas there is a long tradition of research focusing on “why” PNES may develop relatively little research has examined “how” they unfold in the brain. My talk will explore how neuroimaging studies have helped us to conceptualise PNES as a network disorder. While discussing the limitations of the research carried out so far, I will describe the potential of neuroimaging as a diagnostic tool, as a method to explore the heterogeneity of PNES disorders and as an approach to developing new treatments. I conclude that neuroimaging has demonstrated its potential to help with the understanding of PNES but that larger studies with better patient characterisation are needed to make sense of what continues to be a challenging disorder to study.

## Therapeutic drug monitoring for new generation anti-seizure medications

**Behnam Safarpour Lima, MD**

*Neurologist, Epileptologist, Assistant Professor of Neurology, Imam Hussein Hospital, Shahid Beheshti University of Medical Sciences.*

Newer generation anti-seizure medications are increasingly replacing older ones. Therapeutic drug monitoring (TDM) of these medications is one of the controversial topics in epilepsy management. The main purpose of TDM is optimizing treatment outcome, however, studies have shown its usefulness only in appropriate indications including suspicion of noncompliance, unsatisfactory seizure control, pregnancy, elderly, renal or hepatic failure, pharmacokinetic changes, drug interactions and suspicion of toxicity.

methods for TDM of AEDs involve using serum/plasma, saliva, and dried blood spots. Saliva sampling is noninvasive and particularly useful in children. Also, for most ASMs (including levetiracetam) measured concentrations in saliva reflect the free concentration in blood.

Anti-seizure medications therapeutic drug monitoring helps to individualize treatment. many patients may require serum concentrations outside the reference ranges, and thus, patient management is best guided by determination of the “individual therapeutic concentration,” which can be defined as the range of concentrations which has been found to produce the optimal response in the individual patient.



## SUDEP: Risk factors and prevention

**Mehdi Soltani, MD**

*Pars epilepsy center, Tehran, Iran.*

*New Mowasat hospital, Kuwait.*

*Neuromedical center, batonrouge, USA.*

People with epilepsy are at greater risk of early die than the general population. Epilepsy related causes of death in this population account for 40% of the deaths. SUDEP is among the major cause of epilepsy related death after status epilepticus. SUDEP is standing for the sudden, unexpected, witnessed or unwitnessed, non-traumatic and non-drowning death in patients with epilepsy, with or without evidence for a seizure, and excluding documented status epilepticus, in which postmortem examination does not reveal a toxicological or anatomical cause for death. Generalized tonic-clonic seizures are the greatest risk factor for SUDEP; most often, SUDEP occurs after this type of seizure in bed during sleep hours and the person is found in a prone position. Certainly, there are other risk factors including early age onset of epilepsy and male sex, living alone and etc. The exact pathophysiology of SUDEP is currently unknown, although GTCS-induced cardiac, respiratory, and brainstem dysfunction appears likely. Appropriately chosen antiepileptic drug treatment can render around 70% of patients free of all seizures. However, around one-third will remain drug-resistant despite polytherapy. Continuing seizures place patients at risk of SUDEP and reduced quality of life. According to the current data, the best way to prevent SUDEP, is optimizing the control of the seizure by medical or surgical options, educate the patients and care givers and physicians.

In this review, we will discuss about the definition, incidence and importance of SUDEP. We will also try to review some of proposed and possible mechanisms that suggested to explain SUDEP so far. At the end we will review some of the SUDEP's preventive measures.

## What can happen to the heart during video EEG recordings?

**Rainer Surges**

*Department of Epileptology, University Hospital Bonn, Venusberg-Campus 1, 53127 Bonn, Germany.*

The cerebral regions which are involved in the regulation of cardiac autonomic function, including insular cortex, cingulate gyrus, amygdala and hippocampus, are frequently affected by seizure activity, leading to manifold cardiac signs and symptoms in association with epileptic seizures. Sinus tachycardia is the most frequent cardiac expression of epileptic seizures, of benign nature and useful in wearable seizure detection devices. In contrast, ictal asystole is a rare phenomenon which occurs almost exclusively with temporal lobe seizures. Although self-limiting, ictal asystole may be linked to syncope with flaccid falls and injuries. Ictal asystole tends to recur in the same patients, suggesting implantation of cardiac pacemaker if seizure-freedom cannot be achieved. Postictal asystole is also a rare complication of epileptic seizures and appears to occur exclusively following tonic-clonic seizures. In contrast to ictal asystole, postictal asystole is not directly caused by cerebral mechanisms, but secondary to central apnoea and subsequent severe hypoxemia. Postictal asystole is probably the most frequent cause of sudden unexpected death in epilepsy (SUDEP) and may be prevented by early cardiac resuscitation. Postictal ventricular tachycardia was very rarely described following tonic-clonic seizures, and is probably linked to seizure-related alterations of cardiac repolarisation properties.

## **Reproductive disorders in women with epilepsy: The role of anti-seizure medications**

Erik Taubøll

MD, PhD, FEAN. Professor of Neurology

ERGO – Epilepsy Research Group of Oslo. Department of Neurology, Oslo University Hospital  
– Rikshospitalet, Oslo, Norway

Epilepsy, antiseizure medications (ASMs), and the female reproductive system have complex interactions. Hormones affects epilepsy and epileptic activity affects hormones. In addition, ASMs may disturb endocrine function, and reproductive endocrine disorders are unusually common in women with epilepsy.

The use of liver enzyme inducing ASMs (EIASMs) like phenobarbital, phenytoin and carbamazepine increases serum sex hormone-binding globulin (SHBG) concentration. An increase in SHBG leads to diminished bioactive estradiol and testosterone. This may in turn lead to menstrual irregularities and reduced fertility. Most likely, a similar effect on SHBG and then on bioactive hormone levels can be anticipated after all ASMs with varying degrees of enzyme inducing effects. The effect appears to be reversible if an EIASM is replaced by a non-EIASM. EIASMs also reduce the efficacy of hormonal contraceptives which may lead to unplanned pregnancies.

Valproic acid (VPA) have been associated with frequent occurrence of reproductive endocrine disorders in women, characterised by menstrual disorders, polycystic changes in the ovaries and high serum testosterone concentrations (hyperandrogenism). Development of hyperandrogenism and/or ovulatory dysfunction is more pronounced if VPA treatment is started early, before age 26. The changes are probably at least partly reversible when VPA is replaced with i.e. lamotrigine. The mechanism(-s) responsible for the VPA induced effect is not finally settled. Taken together, there are reasons to believe that most of the effect of VPA is mediated peripherally with a direct effect of VPA on steroidogenesis in the ovary resulting in reduced conversion of testosterone to estradiol.

Other ASMs have been studied only sporadically. No clinically significant effects are so far observed with lamotrigine or levetiracetam and both drugs may be good alternatives for women of fertile age.

The endocrine effects of the many newer ASMs have not been widely studied and firm conclusions cannot be drawn. However, it seems that they may in general offer an alternative if reproductive endocrine problems emerge during treatment with the older ASMs.

## Targeting the gut-brain axis for treatment of epilepsy

**Nasim Tabrizi, MD**

*Associate professor of neurology, Mazandaran University of medical sciences, Sari, Iran.*

Epilepsy is a common neurological disorder that could negatively affect quality of life. In about one third of patients, epilepsy is resistant to common antiseizure medications. Thus, various therapeutic approaches have been used for this group with different efficacies. A topic of great interest which recently has lighted a way to new treatment, is the role of gut microbiota in epilepsy. In this review I aimed to investigate the possible role of these micro-organisms in the development and treatment of epilepsy.

Recent studies have suggested an important role for intestinal microbiota in the development of few neurological diseases including multiple sclerosis, Parkinson's disease, Alzheimer's disease and also epilepsy. It has been shown that intestinal microbiota is altered by the ketogenic diet and this alteration is needed to achieve protection against seizure in both human and animal models. Moreover, treatment of animal models by probiotics similar to the intestinal flora which are enhanced by ketogenic diet, has led to seizure protection. There are reports of temporary seizure control in children and adults with refractory epilepsy who received antibiotic therapy. Partial improvement in patients with epilepsy who received probiotics is reported in a recent study as well. The results of these studies possibly could be explained by alteration in gut bacteria. However, well-designed placebo-controlled clinical trials with larger sample sizes and fecal microbiota analysis are necessary to clarify this issue and resolve the contradictions.

## Valproate in treatment of epilepsy in girls and women of childbearing potential

**Torbjörn Tomson**

*Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden.*

Randomized studies have consistently shown that valproate is the most effective antiseizure medication (ASM) for the treatment of generalized tonic-clonic seizures. Unfortunately, its use in the treatment of epilepsy in girls and women of childbearing potential has been limited by its teratogenic potential. Use of valproate during pregnancy has been associated with a high prevalence of major congenital malformations in the offspring as well as with increased risk of adverse neurodevelopmental outcomes including decreased IQ, autism spectrum disorders and ADHD. Due to these risks regulatory agencies such as FDA and EMA have issued firm restrictions for the use of valproate in girls and women of childbearing age, thereby denying many female, unlike male, patients the most effective treatment for their seizure disorder. We will review the details of these regulatory restrictions and their implications for the management of female patients.

## Ultra-high Field Magnetic Resonance Imaging in Epilepsy: Clinical Application

**Gaurav Verma**

*Biomedical Engineering and Imaging Institute, The Icahn School of Medicine at Mount Sinai, New York, USA.*

Multiple magnetic resonance imaging modalities - from T1/T2-weighted structural imaging, to diffusion-weighted and functional MRI - achieve higher signal sensitivity and tissue contrast at ultrahigh field compared to scanning at lower field strengths. Higher sensitivity may in turn be used to facilitate higher spatial resolution in these sequences. Combined with novel post-processing and segmentation techniques, ultra-high field imaging may help to identify subtle imaging markers of pathophysiology. In the context of epilepsy, these sensitivity advantages may help to identify seizure foci undetected on clinical MRI and more widespread and systemic effects of the disease. These imaging markers may facilitate novel interventions like deep brain stimulation, or identify differential effects correlated with seizure frequency or treatment resistance. The high field neuroimaging team at Mount Sinai works across multiple MR imaging modalities and post-processing techniques to image and analyze this complex network disease.

## EEG in the diagnosis and classification of the epilepsy syndromes: clinical practice in adult

**Fatemeh Yourdkhani, MD**

*Neurologist, fellowship of epilepsy.*

After more than 85 years of development and use in clinical practice, the electroencephalogram (EEG) remains a dependable, inexpensive, and useful diagnostic tool for the investigation of the electrophysiologic activity of the brain. Patterns in the interictal EEG make it possible to clarify the differential diagnosis of paroxysmal neurological events, classify seizure type and epilepsy syndromes, and characterize and quantify seizures when ictal recordings are obtained. EEG is an essential component in the evaluation of epilepsy. The EEG provides important information about background EEG and epileptiform discharges and is required for the diagnosis of specific electroclinical syndromes. Such a diagnosis carries important prognostic information, guides selection of antiepileptic medication, and suggests when to discontinue medication.

## Novel pharmacological therapies for epilepsy in the pipeline

**Mohammad Zare, MD**

*Isfahan medical science university, Neurology department, Epilepsy center, Isfahan neuroscience research center.*

Epilepsy is the most common neurological disorder. In spite of medical therapy about 30% of cases are drug resistant. In addition to drug therapy, nerve stimulation, surgery, Gene therapy and stem cell therapy, in recent years other treatment methods are being studied and researched which include: Adjunctive use of P-glycoprotein inhibitors (verapamil, nifedipine, quinidine, amiodarone, nicardipine, quinine, tamoxifen, and cyclosporin A), refinement of chemo genetics consists of using a receptor that detects pathological elevations of the endogenous neurotransmitter glutamate and inhibits neuron, precision medicine to describe medical treatments that target specifically the mechanisms responsible for the manifestations of the disease in individual patients as use of the ketogenic diet to treat glucose transporter 1 (GLUT1) deficiency syndrome and phenytoin for the treatment of epileptic encephalopathies caused by the sodium voltage-gated channel alpha subunit 8 (SCN8A) mutations, Another new treatment method is drug selection based on the recognition of receptors and ion channels, which can include the effect of memantine on the NMDA receptor and quinidine effects on potassium channel. Other research methods under consideration include: using allopurinol, melatonin, Fenofibrate, Minocycline, ceftriaxone, Galanin, TAK 935- OV 936 and everolimus (as modulator of m-TOR pathway in patients with tuberous sclerosis). Although many of the above drugs not yet reached the marketing stage, but is hoped that with the desired result can be of great help in the treatment of epilepsy.



# Posters Presentation

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## Seizure and social outcomes in patients with non-surgically treated temporal lobe epilepsy

Ali A. Asadi-Pooya<sup>1,2\*</sup>, Mahtab Rostamihosseinkhani<sup>1</sup>, Mohsen Farazdaghi<sup>1</sup>

<sup>1</sup> *Epilepsy Research Center, Shiraz University of Medical Sciences, Shiraz, Iran.*

<sup>2</sup> *Jefferson Comprehensive Epilepsy Center, Department of Neurology, Thomas Jefferson University, Philadelphia, PA, USA.*

**Background:** To investigate the seizure outcome with medical treatment in patients with temporal lobe epilepsy (TLE) and its associated factors. We also investigated the social outcome of the patients.

**Methods:** This was a retrospective study of a prospectively built electronic database of patients with epilepsy. All patients with a diagnosis of TLE were studied at the outpatient epilepsy clinic at Shiraz University of Medical Sciences, Shiraz, Iran, from 2008 until 2019. In a phone call to the patients, at least 24 months after their diagnosis at our center, we investigated their current seizure control and social status.

**Results:** Two hundred and twenty-two patients were studied, 101 patients (45.5%) were seizure free. A lower number of the prescribed drugs was the only factor with a significant association with the seizure free outcome (Odds Ratio: 1.460,  $p = 0.001$ ). At the time of the phone call, 76 patients (37.6%) reported having a college education, 103 patients (51%) were employed, 146 patients (72.3%) were married, and 81 patients (40%) reported driving a motor vehicle. The employment status, college education, and driving a motor vehicle were significantly associated with a seizure-free outcome status. The social achievements of the patients, who were partially responsive to medical therapy, were significantly worse than those who were seizure free.

**Conclusion:** Many patients with TLE may suffer from drug-resistant seizures. Ongoing seizures in these patients may affect their social lives substantially. Seizure reduction (not freedom) is not good enough to help the patients with TLE enjoy a healthy life with satisfactory social achievements.

**Keywords:** Epilepsy, Temporal lobe, Seizure, Outcome, Social.

## Effect of hydro-alcoholic extract of *Matricaria recutita* L. on pentylenetetrazole-induced kindling and some biochemical parameters in male mice

Mohammad Amin Farzin<sup>1</sup>, Maryam Kazemi<sup>2</sup>, Gholamreza Ghavipanjeh<sup>2\*</sup>

<sup>1</sup>Department of Medical Laboratory Sciences, Kashan University of Medical Sciences, Kashan, Iran.

<sup>2</sup>Department of Medical Physiology, Kashan University of Medical Sciences, Kashan, Iran.

**Background:** As *Matricaria recutita* (MAT) comprises a series of flavonoid compounds with benzodiazepine-like properties, it may be effective in the treatment of epilepsy and seizure disorders. In this study, the effect of intraperitoneal injection of hydro-alcoholic MAT extract on seizure induced by pentylenetetrazole (PTZ) in mice was evaluated.

**Method:** Utilizing a PTZ-kindling model, 48 male mice (25-30 g) were divided into 6 groups (n= 8): Saline, Control (PTZ-treated), MAT (50 mg/kg), MAT (400 mg/kg), Valproate (150 mg/kg), Valproate (50 mg/kg)+ MAT (50 mg /kg). The seizure threshold was evaluated as a criterion for kindling. In addition, nitric oxide metabolites (NOx) and malondialdehyde (MDA) were measured in the brain tissue.

**Results:** Since MAT enhanced the seizure threshold, it revealed an anticonvulsant property. Moreover, MAT significantly increased MDA levels in the brain, whereas it decreased the levels of NOx.

**Conclusion:** The hydro-alcoholic extract of MAT has an inhibitory effect on PTZ-induced seizures. The extract also decreased and increased NOx and MDA levels in the brain, respectively.

**Keywords:** German chamomile, Kindling, Pentylenetetrazole, Nitric oxide, Malondialdehyde.

## The effect of family-centered care on the family caregivers' burden of patients with epilepsy

Nahid Jivad<sup>1</sup>, Zahra Forouzandeh shahrakei<sup>2</sup>, Maryam Heydari<sup>3</sup>, Shahram Etemadifar<sup>4</sup>, Reza Masoudi<sup>5</sup>

<sup>1</sup>Assistant Professor, Department of Neurology, Faculty of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran.

<sup>2</sup>Research Expert of Shahrekord University of Medical Sciences, Shahrekord University of Medical Sciences, Shahrekord, Iran.

<sup>3</sup>Instructor, Community-Oriented Nursing Midwifery Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran.

<sup>4</sup>Assistant Professor, Community-Oriented Nursing Midwifery Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran.

<sup>5</sup>Professor, Department of Epidemiology and Biostatistics, Faculty of Health, Shahrekord University of Medical Sciences, Shahrekord, Iran.

**Background:** Caring for patients with epilepsy, creates many challenges for their family caregivers. The implementation of family-based interventions can facilitate the caring duty of caregivers and increase the quality of care for patients. This study aimed to investigate the effect of family-based care program on care burden in family caregivers of patients with epilepsy.

**Method:** This clinical trial study was conducted in Ayatollah Kashani and Hajar hospitals in Shahrekord City, Iran for 7 months in 2016. Samples were selected by convenience sampling method and randomly assigned in the intervention (n=50) and control (n=50) groups. For the intervention group, a family-centered care program was implemented including self-efficacy, self-esteem and evaluation, through education, support, problem solving and group discussion during four sessions. Data were collected by using Persian version of Zarit's burden of care scale from the intervention and control groups in three stages, before, immediately, and two months after the intervention. Data were analyzed by descriptive and analytical t-test and ANOVA with repeated measurement in the SPSS.

**Results:** The mean score of burden of care in the intervention and control groups were 37.42 and 34, respectively before the intervention ( $P < 0.179$ ). The mean score of care burden in the intervention and control groups immediately after the intervention was 21.36 and 28.7, respectively and two months after the intervention was 15.78 and 27.92 respectively

**Conclusion:** The results showed that a simple, low-cost and feasibility program of family-based care has significantly reduced the care burden of caregivers of epilepsy patients. This family centered program can help to play a better role for family caregivers with physical and psychological stress.

**Keywords:** Family caregivers, Family-centered care, Epilepsy, Burden, Iran.

## Effects of family-centered empowerment intervention on stress, anxiety, and depression among family caregivers of patients with epilepsy

Nahid Jivad<sup>1</sup>, Zahra Forouzandeh shahrakei<sup>2</sup>, Shahram Etemadifar<sup>3</sup>, Reza Masoudi<sup>4</sup>, Maryam Heidari<sup>5</sup>

<sup>1</sup>Assistant Professor, Department of Neurology, Faculty of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran.

<sup>2</sup>Research Expert of Shahrekord University of Medical Sciences, Shahrekord University of Medical Sciences, Shahrekord, Iran.

<sup>3</sup>Assistant Professor, Community-Oriented Nursing Midwifery Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran.

<sup>4</sup>Professor, Department of Epidemiology and Biostatistics, Faculty of Health, Shahrekord University of Medical Sciences, Shahrekord, Iran.

<sup>5</sup>Instructor, Community-Oriented Nursing Midwifery Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran.

**Background:** Family caregivers face numerous challenges in taking care of their family members with epilepsy. The empowerment of this group of people, who can be described as forgotten patients, should always be considered through supportive interventions; therefore, this study investigated the effect of a family-centered intervention program on stress, anxiety, and depression among family caregivers of patients with epilepsy

**Method:** In 2017, a trial was conducted in Iran among subjects selected by the convenience sampling method and randomly assigned to two groups: intervention and control. After five sessions per week over a four-week period, the intervention- and control-group data were collected using the Depression Anxiety Stress Scale (DASS) in three stages: before, immediately after, and two months after the intervention. Data were analyzed with Statistical Package for the Social Sciences (SPSS) software using descriptive and analytical statistics, an independent *t*-test, and repeated measures Analysis of variance (ANOVA).

**Results:** In this study, the family caregivers included 61.3% women and 38.7% men, with a mean age of 37.5 years. The findings showed no significant differences in the mean scores of stress ( $p=0.93$ ), anxiety ( $p=0.91$ ), and depression ( $p=0.56$ ) before the interventional program between the intervention and control groups, but these differences were statistically significant in the mean score of stress ( $p=0.003$ ) in the immediately after the interventional program, whereas the mean scores of depression were not decreased significantly ( $p=0.3$ ). Two months after the interventional program the mean scores of stress ( $p=0.001$ ) and anxiety ( $p=0.001$ ) were significantly decreased in the intervention group, but the mean score of depression was not decreased significantly ( $p=0.09$ ).

**Conclusion:** The results suggested that a family-centered intervention program reduced the stress, anxiety, and depression of caregivers because of feasibility, simplicity, and utility of intervention. This program was focused on psychological issues of caregivers, and an emphasis on their empowerment helped them in managing their problems in the caregiving situation and achieved greater psychological potency in the caring process.

**Keywords:** Epilepsy, Family caregivers, Stress, Anxiety, Depression, Iran

## Evaluation of the need to combine 18F-FDG PET imaging modality with other imaging modalities in preoperative evaluation of drug-resistant epilepsy patients

Fatemeh Khosrobeygi Bozcheloie

*Preclinical Lab, Core Facility, Tehran University of Medical Sciences.*

**Background:** PET imaging systems often have a wider distribution than seizure foci that can show both the center and areas of seizure prediction activity, but despite the high sensitivity, do not provide acceptable results alone. This review examines whether FDG-PET in combination with other methods is useful in preoperative evaluation.

**Method:** The present review study was conducted by searching the Pubmed, Science Direct, Google Scholar, Magiran and SID databases in Persian and English since 2014. Finally, among the searched articles, 25 articles were used based on the study criteria.

**Results:** The results include the following: 1) The need for intracranial EEG monitoring is reduced due to increased confidence in localization before surgery. 2) The addition of SISCOM is useful in cases where the epileptic lesion is undiagnosed and the MRI findings are abnormal. 3) It is useful for accurately guiding (SEEG) electrode implantation. 4) Helps to better understand the pathophysiology of epilepsy, shows focal abnormal metabolic regions, classifies the functional state of the brain, and defines its functional integrity.

**Conclusion:** The use of multimodal imaging at the same time, with better patient selection, lower cost, lower risk, and better surgical outcomes, will help as part of preoperative evaluation in patients evaluated for refractory epilepsy surgery. Finally, the proper use of these tests, combined with more comprehensive functional mapping of the brain, may lead to the evaluation of completely non-invasive epilepsy surgery.

**Keywords:** Drug-resistant epilepsy, pre-surgery, Multimodal imaging, <sup>18</sup>F-FDG PET, Review.

## Quality of life in children with epilepsy

Adeleh Rahimpour Moradi

*Department of Rehabilitation management, Faculty of Rehabilitation, Iran University of Medical Science, Tehran, Iran.*

**Background:** Epilepsy is a chronic neurological disease that can have debilitating and undeniable effects on various aspects of life, including psychological, social, and physical dimensions, and affect one's quality of life. Because of the high prevalence of this disease among children, concerns about their quality of life are greater and need more detailed investigation.

**Method:** To review previous studies using keywords such as childhood epilepsy, quality of life, and pediatric in three Google Scholar databases, PubMed, Scopus, we searched from 2010 to 2022. According to the inclusion and exclusion criteria, eight studies were chosen.

**Results:** Three studies showed that as age increases, the quality of life decreases significantly. This may be due to children's self-awareness about the disease and its negative aspects. Educational problems, decreased self-esteem, decreased independence, and reduced social participation are common consequences among these children. The psychological problems caused by this disease can lead to decreased physical activity, poor muscle strength, and physical decline. The age of the child, the time of the first seizure, performance, and family support significantly affect the quality of life of these children.

**Conclusion:** According to the findings, epilepsy affects a wide range of children's lives, and due to the sensitivity of this age group, the management of this disease in an appropriate way plays an important role in improving the quality of life and should be considered.

**Keywords:** Childhood epilepsy, Quality of life, Pediatric.

## Frequency of acute symptomatic seizures in adult hospitalized patients

Sheida Shaafi<sup>1</sup>, Ali Mohammadian negad, Mehdi Hemmati

<sup>1</sup> *Associated Professor of Neurology, Tabriz University of Medical Science.*

**Introduction:** acute symptomatic seizures (ASS) are considered as one of the medical emergencies. The causes of ASS in developed countries may differ from the causes in developing countries. The aim of our study was to determine etiological risk factors of adult medical admissions due to ASS in our community. Investigating these factors could be useful in providing better prevention and control of seizures.

**Method:** This study is a cross-sectional study (in a period of three years) by total sampling method, in non-traumatic patients admitted to the neurology ward with diagnosis of ASS. Demographic data, information about the patient's type of seizure, underlying diseases, drug history, systemic and neurological examination findings, routine laboratory data and EEG findings were gathered. Then data was analyzed with SPSS and statistical tests (P-value < 0.05)

**Results:** From 200 patients with mean age 49.6 (29-70) years old, 52% were male and 48% were female. 45% of patients had a history of underlying diseases such as hypertension, diabetes, renal disease, stroke, immunosuppressive diseases and intravenous drug abuse and the most common disease was hypertension (20.5%) followed by diabetes (12%), stroke, renal disease, immunosuppressive diseases and drug abuse.

**Conclusion:** According to our results, stroke and infectious diseases were the leading causes of ASSs in adults.

**Keywords:** Symptomatic, Seizure, Adult.



## Epilepsy and pregnancy: Latest news, Do's and Don'ts

**Sheida Shaafi**

*Associate Professor of Neurology, Department of Neurology, School of Medicine,  
Tabriz University of Medical Sciences, Tabriz, Iran.*

**Introduction:** Epilepsy and pregnancy is one of the most challengeable topics in epilepsy management and both for the epileptologist and patients is very stressful.

**Methods:** This review will outline risks for epilepsy during pregnancy, first seizure in pregnancy, and provide an evidence-based approach for managing patients with epilepsy before, during, and after pregnancy. This is a systematic review about this topic in recent five years.

**Results:** Despite differences in methodology, all registries have reported similar findings and have all noted that exposure to VPA poses the greatest risk for MCMs. They have also shown that both lamotrigine and levetiracetam have a relatively low potential. Polytherapy has been shown to increase the risk for major congenital malformation and monotherapy is preferred.

Neurodevelopmental finding showed increased risk of autism spectrum disorders and significantly reduced IQ scores with VPA in comparison to other ASMs. Changing medications while pregnancy exposes the patient and her fetus to the unknown effectiveness of the new ASM and placing the woman at risk of having seizures that may be a cause of fetal asphyxia, bradycardia, direct injury also mortality.

**Conclusion:** Epilepsy is not a contraindication to pregnancy. Successful management of these pregnancies therefore ideally involves pre-pregnancy consultation and close collaboration between the obstetric and neurology providers as a multidisciplinary team.

**Keywords:** Epilepsy, Pregnancy, Management.