

July - September 2019

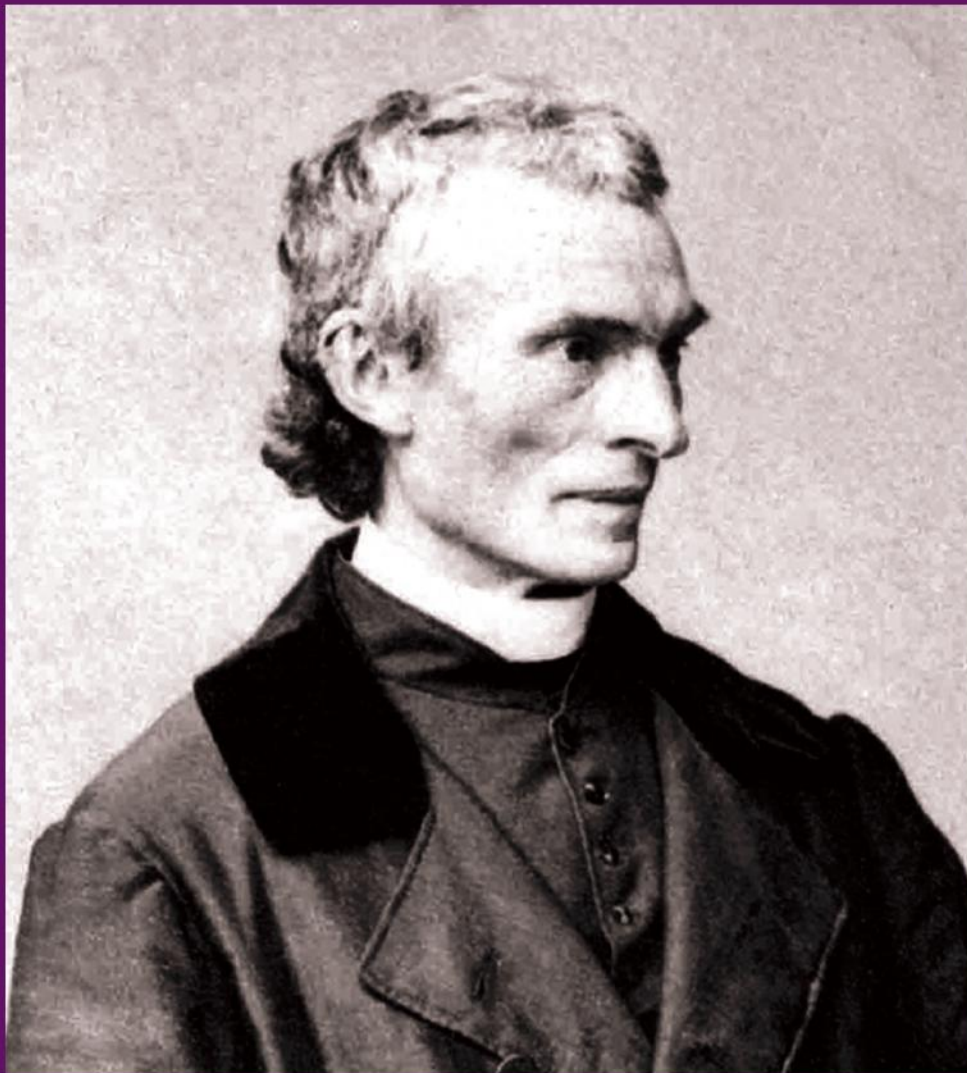
Issue 3, 2019

Epilepsy India



Newsletter of the Indian Epilepsy Association & Indian Epilepsy Society

Pierre Eymard



Valproic acid – A serendipitous discovery



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EDITORIAL OFFICE :

16-7-129, Ramamurthy Nagar,
2nd Street, Minibyepass Road,
Nellore 524003
neurology.nellore@gmail.com

Editorial...



Dr. Bindu Menon



Dr. Chanda Kulkarni

Greetings from the editorial team,

The cover page in this issue features and introduces **PIERRE EYMARD** the French researcher who fortuitously discovered anticonvulsant activity of Valproic acid in 1962. VPA is now established as a major anti-epileptic drug across the world for various types of epilepsy and is included in the WHO's list of essential medications.

Mr. Anand K Khatiwora shares with us a story of a woman with epilepsy, her journey from a faith healer to the proper treatment. Misconceptions about epilepsy are the greatest barrier to epilepsy. The article also describes that with proper treatment patients can be seizure free and lead a normal life. Thanks for sharing the heart-warming story. **Dr. Sanjeev Thomas has been the proud recipient of the prestigious Ambassador for Epilepsy Award at the 33rd International Epilepsy Congress BANGKOK 2019.** Hearty congrats and very well deserved.

We continue our drug corner where Dr. Amrutha Thomas and Dr. Arya Gigi give us an overview of the pharmacological profile of Lacosamide.

Indian epilepsy school was held at Jodhpur, which included prominent international and national faculty covering a wide range of topics. Included is a report.

Bangalore chapter has come out with a book "Hand book on Epilepsy". The book is a comprehensive read covering all the aspects of epilepsy. So don't forget to grab a copy for your own library.

Grants are being announced by the IEA 18th International congress trust in the field of social and research activities. Please read the guidelines and submit your proposals. We once again submit the guidelines for submission for the EI newsletter. We request all the members to adhere to the guidelines so that we can publish maximum reports and articles.

And finally we are fast approaching our next annual conference ECON 2020 at Ahmedabad, India's first world heritage. Three days of learning, debates CPC, Quiz and much more. Don't forget the last date of Abstract submission and register in large numbers and have a great learning experience.

Keep doing good work and share it with us for EI newsletter.

ME AND MY EPILEPSY



MR ANAND K. KHATIWORA

EEG (Neuro) Technologist, Department of Psychiatry
STNM Hospital, Gangtok, Sikkim India, 737101

Let me introduce Mrs. Pema Choki, 50 yrs undoubtedly, she is one of the strongest women I have ever met. Self-employed, she runs her own grocery shop and is also a proud mother of three children. By appearance, she looks, strong, bold and satisfied with her life.

I first met her at the hospital; she had come for her follow up appointment with her doctor. She was standing outside the clinic and I asked how I could help her. She mentioned that she was here to meet her doctor and saying so she handed her OPD card to me. I saw that she was on treatment for epilepsy.

Somehow, I felt like talking to her in greater detail as also knew that her doctor would be at morning rounds in the ward and would take some time before he came to the clinic.

I asked her if I could talk to her for a while and after a brief pause she agreed. I ushered her to EEG room and offered her a chair.

After she was comfortably seated and at ease, I started by mentioning that it seemed she had been on treatment for epilepsy for quite a long time just by glancing at the thick pile of OPD cards she was holding. I proceeded to ask her when she had started taking treatment and how her life has been since then?

I could see from her facial expression that she was a bit nervous and excited hearing my question.

After taking a long breath, she started:

"Sir, I was diagnosed to have epilepsy when I was about 22 years. I had already had 2-3 seizure attacks prior to that which my family and I ignored thinking it was due to physical weakness. After the fourth attack, my father took me to a faith healer to whom he narrated what my problem was. After carefully listening to my father, the faith healer nodded his head and seemed that he was aware and fully cognizant of what was going on with me. He asked me to sit on the chair and started his rituals which included sprinkling some water on me, then some rice followed by more sprinkling of substances of varied colors. This procedure took almost half an hour after which he informed my father that some evil spirit had been trying to possess me, that he had done all the necessary prayers and rituals to rid me of this evil possession. Further, he assured my father that there was nothing not to worry about since he had taken the required remedial steps. He blew some air into a fistful of rice in his hand and gave it to my father with a direction – "make your child eat four grains of rice three times a day for fifteen days".

After hearing that every thing had been taken care of, we were grateful for the faith healers service and my father paid him in cash and also made an offering of a basket full of dry fruits. As he received the basket of dry fruits he added that if it (seizure) happens again we should visit him early morning on a full moon day. We walked back home, my father more satisfied and relieved than me. He continued to praise the faith healer as we made our way back home. Everyone at home was eagerly waiting for our arrival; the

atmosphere hung about as if I was coming back with my graduation result. As we entered home, we were bombarded with questions from my mother and other family members. "What did the faith healer say? What did he do for you? Is it cured now? My father painstakingly explained everything in great detail.

So from that day, I had additional things to do, i.e. to eat four pieces of rice, morning, noon and evening. Every day, my mother asked me whether I ate the rice or not. I diligently ate the rice at the instructed times and had no attacks and even I started to develop faith on the faith healer.

Then, soon enough it was New Years Eve and my family decided to host a party. We invited a number of close relatives and friends. I was happy and excited; we planned to stay up until we ushered in the New Year. I helped my mother in the preparation of various dishes and serving our guests. After dinner, we had a bonfire on our yard. We had great fun singing, dancing and playing games like truth and dare. Finally, it was 12:00 am and we wished everyone for the New Year. Our parents asked us to go to bed then but few of my cousins pleaded that we be allowed to stay till morning as we seldom met as a whole family. Our request was granted and overjoyed; we sang and danced through the night. Undoubtedly, it was one of the best times spent with my cousins.

Next day relatives left, now it was me and my mother taking care of the home, cleaning, washing dishes etc.

That very day i.e. 1st Jan afternoon, I had three attacks of seizure on that single day. It was unexpected, I was scared and I could sense that my parents panicked. I remember very little what all happened after that. It was only on the next day that I could gain full consciousness. I woke up to find myself lying in the bed the same faith healer talking to my family members. I heard him saying –"she was outside last night the evil spirit possessed her again".

My parents scolded me for staying outside for the whole night; I was still groggy and lethargic.

That evening, one of our distant relatives- an uncle, happened to visit us at home. When he came to know that I was not feeling well, he asked what happened. My mother narrated what I had been experiencing with tears in her eyes. After listening to my mother's narration, my uncle advised us to see a doctor at once. He had read and heard about seizures being treatable. Next morning my father, along with my uncle took me to the city hospital to see the doctor. It took a couple of hours to get there and I was quite apprehensive during the journey to the hospital. My father narrated what had been happening to me. The doctor asked me in detail and my parents as they were witness to my attacks and said that my symptoms and episode were that of "Epilepsy". He advised us that I undergo two investigations-EEG (Electroencephalograph) and MRI (brain). Further, he prescribed medicine and explained how to take the medicine and its timings. He also stressed that I should not skip a single dose or stop medication without his advice.

I was quite curious as to how I was getting these attacks and moreover, the faith healer had said I was possessed by some spirit. The doctor explained that I was getting these attacks because of abnormal electrical activity of the neurons in the brain and nothing else. He also explained that this was a treatable illness and that I would get better if I complied with the medication regimen faithfully. Hearing this, I was quite relieved. Also, I did not want to be possessed by a spirit of all things! He asked me to visit the clinic again with the reports of the investigations he had advised.

I underwent a MRI Brain and EEG Test and visited the doctor after two days. Looking at the report, the doctor confirmed that I was suffering from epilepsy.

Thereafter, the doctor told me that there were couple of dos' and don'ts for a person with epilepsy which I still remember very clearly.

DO's

- 1) Consult your treating doctor regarding your medicine.
- 2) Have adequate sleep at night.
- 3) Eat meals regularly and
- 3) To take medicine on time.

Don'ts

- 1) Do not go swimming.
- 3) Do not ingest alcohol or any substance that causes intoxication.
- 4) Do not cook in open fire when alone

"I immediately decided that I take my medications regularly and interestingly since that day, for the last 23 odd years, I haven't experienced a single episode of seizure. I am really thankful to my treating doctor and the medicines for making me feel that epilepsy is no different from any other ailment such as hypertension or diabetes if treatment is taken on time and according to the doctor's advice."

As she narrated her experience with epilepsy, I could perceive how confident and satisfied she currently was.

As we still had some time, I further asked her about her family and how important is the role of family in supporting her was?

She began with: "I am a proud mother of three children. My eldest is a son an engineer, daughter is married and the youngest is doing her university studies."

She then continued and said – "Having epileptic attacks is not just a convulsion, loss of consciousness and coming back to normal life. Sometimes, she has mood swings and frequently feels irritable. During these times, she needs support from her family and friends and she is very lucky to have such a wonderful group of people in her life. She has a very supportive husband and family. Her husband was aware of her having epilepsy and medications before they got married. She is lucky that he responded in a very positive manner, comforting her by saying, even he is taking medicine for his hypertension. He has been truly her pillar of strength at all times. She added that if a person has supportive environment, half the complications vanish and that one gets the courage to face life come what may".

Finally, I asked her if she had to advice any person with epilepsy, what she could advise.

(She): "I am not an expert on epilepsy but still if you ask me about my experience I would say-

No one knows your epilepsy better than your treating doctor (listen to everyone but follow only your doctor's advice).

As doctors can't be with you 24x7 and medication has its own limitation, I have learnt as a patient one should

have own dos' and don'ts already mentioned earlier as well as the medicine to stay seizure free. Like –

- Take your medicine regularly without skipping or stopping until and unless your doctor advises you to do so
- Do not deprive your sleep
- Avoid stressful situation as much as possible.
- Take adequate rest.

Just as she finished, it was her turn to meet the doctor. I thanked her for her time and for sharing her personal experience with me. I also asked her permission to share her story so that it could in some way inspire others with epilepsy and she readily agreed!

I do this whenever I get an opportunity similar to the one that I tried with Ms. Prema Choki in this article.

Congratulations



Ambassador for Epilepsy Award 2019

Dr. Sanjeev Thomas received the **prestigious Ambassador for Epilepsy Award at the 33rd International Epilepsy Congress BANGKOK 2019**

Dr. Sanjeev Thomas is the President of Indian Epilepsy Society, member of the ILAE Commission on Medical Therapy of Epilepsy, the Women and Pregnancy Task Force, and the new ILAE-Lancet Neurology Commission (all for 2017- 21).

DRUG CORNER

PHARMACOLOGICAL PROFILE OF LACOSAMIDE

Dr. Amrutha Thomas, Dr. Arya Gigi and Dr. Chanda Kulkarni.
SAKRA World Hospital, Bangalore.



Dr. Amrutha Thomas
Pharm D, Clinical Pharmacist



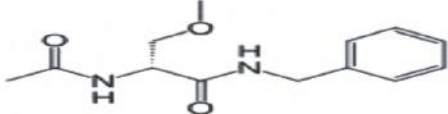
Dr. Arya Gigi
Pharm D, Clinical Pharmacist

INTRODUCTION

Lacosamide (LCM) was discovered by Dr. Harold Kohn, Dr. Sridhar Andurkar, and colleagues at the University of Houston in 1996 and was subsequently approved by the US Food and Drug Administration in 2008 as adjunctive therapy for focal onset seizures in patients of 17 years of age and older. The efficacy of this agent in adults subsequently led clinicians to consider lacosamide for children aged 4 years and older with partial-onset seizures as monotherapy or adjunctive therapy.

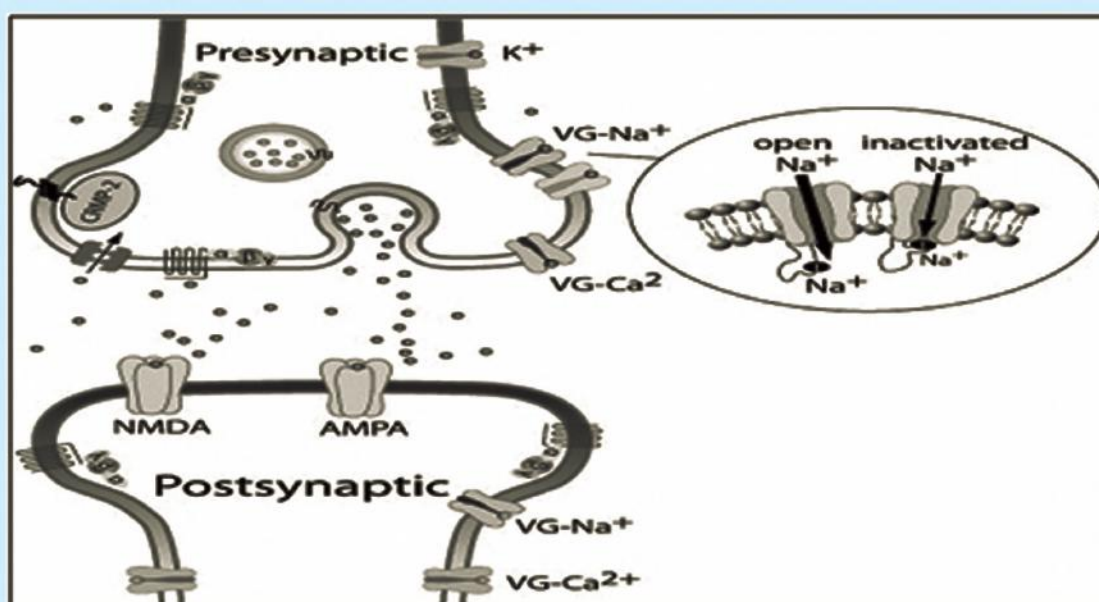
Its unique **mechanism of action**, lack of **significant drug interactions**, relatively **mild adverse effect profile**, and availability in an intravenous (IV) dosage form have made lacosamide a useful addition to treatment with traditional antiseizure drugs. Intravenous (i.v.) LCM has safety and tolerability similar to that of oral LCM. LCM is mainly prescribed in outpatient epilepsy or neurology clinics.[2] However, its favorable pharmacokinetic profile, good tolerability, possibility of fast titration and IV formulation suggest that it may be a very useful drug to use in hospitalized patients.

Table 1

Synonyms	<ul style="list-style-type: none"> (2R)-2-(acetyl amino)-N-benzyl-3-methoxypropanamide 
Routes of administration	<ul style="list-style-type: none"> Oral, <u>Intravenous</u>
Elimination half-life	<ul style="list-style-type: none"> 13 hours
<u>Excretion</u>	<ul style="list-style-type: none"> Renal
Indication	<ul style="list-style-type: none"> Partial-onset seizures Diabetic neuropathy and small fibre neuropathy
Dosage forms and strengths	<ul style="list-style-type: none"> 50 mg (pink), 100 mg (dark yellow), 150 mg (salmon), 200 mg (blue) film-coated tablets 200 mg/20 mL single-use vial for intravenous use

MECHANISM OF ACTION ^[4]

LCM is a functionalized amino acid that selectively **enhances slow inactivation of voltage-gated sodium channels**, increasing the proportion of sodium channels unavailable for depolarization. This enhancement of the slow inactivation of the voltage-gated sodium channels produces stabilization of neuronal membranes and inhibition of sustained repetitive neuronal firing (Figure 1). Unlike other anticonvulsants, including carbamazepine, felbamate, lamotrigine, oxcarbazepine, phenytoin, and topiramate, **lacosamide does not alter fast inactivation of voltage-gated sodium channels**. Lacosamide may also interact with collapsing response mediator protein 2 (CRMP-2);⁴ however, this binding has recently been challenged.⁵ CRMP-2 is part of a signal transduction cascade of neurotrophic factors involved in neuronal differentiation, regulation of gene expression, polarization, and axonal outgrowth. It has been proposed that **binding at CRMP-2 could produce a neuroprotective effect, reducing glutamate-induced excitotoxicity and enhancing the clinical efficacy of lacosamide**.



(Figure 1). Mechanism of Action of Lacosamide

AMPA, α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor; K, potassium; NMDA, N-Methyl-D-aspartic acid; VG-Ca²⁺, voltage gates calcium channels; VG-Na⁺, voltage gates sodium

DOSING

MAXIMUM DAILY DOSAGE FOR EPILEPSY AND DIABETIC NEUROPATHY ^[3]

Adults ^[1]

400 mg/day PO or IV.

Geriatric

400 mg/day PO or IV.

Adolescents

17 years: 400 mg/day PO or IV.
13 to 16 years and weighing 50 kg or more: 400 mg/day PO.
13 to 16 years and weighing 30 to 49 kg: 8 mg/kg/day PO.
13 to 16 years and weighing 11 to 29 kg: 12 mg/kg/day PO.

Children

4 to 12 years and weighing 50 kg or more: 400 mg/day PO.
4 to 12 years and weighing 30 to 49 kg: 8 mg/kg/day PO.
4 to 12 years and weighing 11 to 29 kg: 12 mg/kg/day PO.
1 to 4 years: Safety and efficacy have not been established.

DOSING CONSIDERATION ^[5]

Renal Impairment

- CrCl 30 mL/minute or more (adults) or CrCl 30 mL/minute/1.73m² or more (pediatrics):
No dosage adjustments are needed;
- CrCl less than 30 mL/minute (adults) or CrCl less than 30 mL/minute/1.73m² (pediatrics) or end-stage renal disease: 25% reduction of the maximum dosage; use caution with dose titration.

COMMON ADVERSE EFFECTS ASSOCIATED WITH LACOSAMIDE ^[4]

Dizziness, Headache, Diplopia Nausea & Vomiting, Fatigue, Blurred vision, Ataxia, somnolence, tremor, nystagmus

REFERENCE

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4. Marcia L. Buck, PharmD^{1,2} and Howard P. Goodkin, MD, PhD. Use of Lacosamide in Children with Refractory Epilepsy. J Pediatr Pharmacol Ther. 2012 Jul-Sep; 17(3): 211–219.
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INDIAN EPILEPSY SCHOOL 2019

Reported By : COURSE DIRECTOR DR. SAMHITA PANDA

The Indian Epilepsy School 2019 was held in Jodhpur, from 22nd to 25th August 2019 (Thursday to Sunday). This residential school was organised jointly by the Departments of Neurology, All India Institute of Medical Sciences, Jodhpur and Dr. S.N. Medical College, Jodhpur under the aegis of Indian Academy of Neurology and the Indian Epilepsy Society. Dr. Amita Bhargava was the Organizing Chairperson and Dr. Samhita Panda was the Organizing Secretary of the IES 2019. The aim of the Indian Epilepsy School 2019 was to enhance and update knowledge about management of epilepsy, establish a good level of confidence in reading EEGs, providing delegates the chance to come together, discuss the latest developments in basic and clinical epileptology, and network with fellow researchers and renowned teachers in the field of epileptology. This holistic update of knowledge in various aspects of epilepsy targeted the neurology residents and young neurologists.

The faculty were 40 eminent neurologists and epileptologists from across India. There were 2 overseas faculty- Dr. Goran Lantz, University of Geneva, Switzerland and Dr. Nitin Sethi, New York-Presbyterian Hospital, New York. A total of 60 delegates from all over the country participated in the 3 and half day long school.

The school comprised of group learning sessions covering topics of epilepsy as well as hands-on EEG/video-EEG learning. The delegates and faculty (as mentors) were divided into small groups to encourage self learning, discussions and direct interactions with the experts. The topics discussed during the group learning sessions included Classification of Seizures and Epilepsies, Symptomatic Epilepsy & its substrates, Newer AEDs on the block, Discontinuation of AEDs, Neonatal and childhood epileptic encephalopathies, Women with Epilepsy, Outcomes after Epilepsy Surgery and Status Epilepticus. In addition, 27 lectures were also taken covering a range of topics from basics of epileptogenesis and networks to presurgical evaluation and surgical options of drug refractory epilepsy.

The hands-on EEG and video-EEG in groups covered topics including electrodes, montages & activation procedures, EEG artefacts and benign variants, focal and generalized EEG patterns and semiology and ictal patterns of temporal and extratemporal lobe epilepsy. A live demonstration of High density (256 channels) EEG with a preceding lecture on Presurgical evaluation using Electrical Source Imaging generated a lot of interest amongst the audience.

Another highlight was the panel discussion on SUDEP which helped cleared many doubts among the delegates.

A Quiz was held on the last day of the school with the purpose of self assessment as well as to encourage the delegates. The Quiz masters were Dr. Ashalatha.R from SCTIMST, Thiruvananthapuram and Dr. Pramod Krishnan from Bengaluru. The first prize was won by Dr. Shivan Kesavan from Chandigarh, second prize by Dr. Jason Ambrose F. from Tirunelveli, third prize by Dr. Aparajita Chatterjee from Bengaluru and fourth prize by Dr. Ch. Anusha from Vishakhapatnam. The prizes included cash prize with book prize and certificate.

The overall experience by the delegates and the faculty was fulfilling as provided by the feedback received. Most appreciated the group activities and preferred this modality of teaching for both the theoretical aspects as well as EEG, and hoped this trend will be continued in the subsequent years.

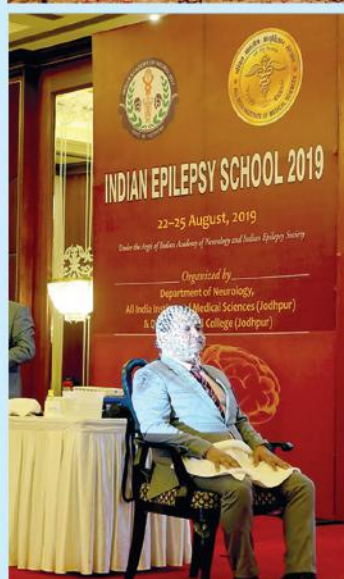


Fig. 1: Inaugural ceremony of the Indian Epilepsy School 2019 with chief guest Prof. S.S.Rathore, Principal of Dr. S.N. Medical College and Guest of Honour Prof. M. Gourie-Devi

Fig. 2: Lamp lighting at the Inaugural ceremony

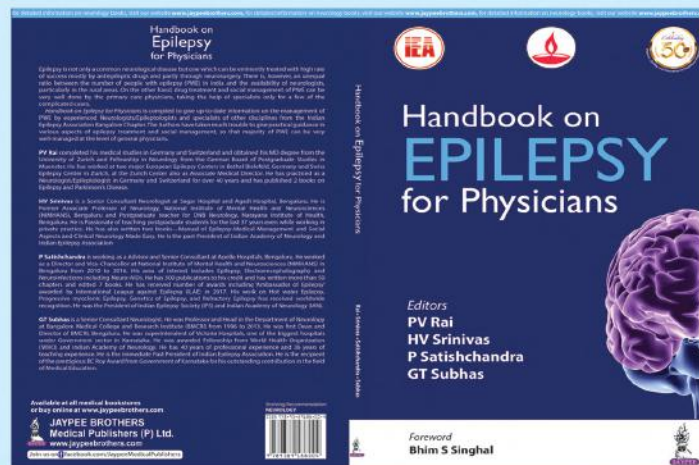
Fig. 3: Demonstration of high-density EEG for Electrical Source Imaging

Fig. 4: Group Photo of IES 2019

CHAPTER ACTIVITIES

BANGALORE

Reported By : DR H V SRINIVAS.



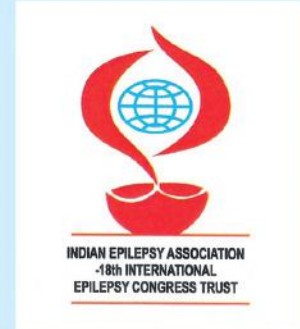
Indian Epilepsy Association Bangalore chapter(IEA) has come out with a book "Hand Book on Epilepsy - for Physicians". The book comprises of several chapters written by specialists who are members of the IEA Bangalore Chapter. The book begins with short history of epilepsy and covers seizures during various stages of life – children, adults, womenand elderly. Further discussions are on diagnosis, investigations,emergency treatment, therapeuticmanagement, including therapy resistant epilepsy, surgery.Also covered are psychiatric, genetic aspects, counselingand prevention of epilepsy. In keeping with the objectives of IEA, social aspects of epilepsy are well covered e.g. Epilepsy and Law, education, employment, diet, T.V etc. The book concludes with a brief history and activities of IEA Bangalore Chapter.

The book was released on 31st May 2019 during KAPICON 2019 (Karnataka State API Conference) at Belgaum, an appropriate forum where Karnataka State Physicians were assembled.

ANNOUNCEMENT

Indian Epilepsy Association-18th International Congress Trust (The Trust), New Delhi established in 1991 and registered under Indian Registration Act on 09 April 1993 provides financial grants from time to time. The grants are made available to all valid members of Indian Epilepsy Association and its State Chapters and members of Indian Epilepsy Society.

The areas in which grants are offered are inter alia
Promoting epilepsy studies and health care
Actions towards awareness of epilepsy
Promoting social services for those affected by epilepsy
Travelling fellowships domestic and international
Holding of workshops, symposium, conferences etc. devoted to epilepsy
Helping towards research on social and medical aspects of epilepsy



The entitled members may approach the Trust with an outline of their proposal.
The Trustees for approval of the financial grant will judge suitability of such applications.
The Application Blank may be obtained from the Office of the Trust.

Dr VS Saxena
Secretary
Indian Epilepsy Association-18th International Congress Trust
K10 DLF City-II, Gurugram 122002
0124-4363035/36, 9811050030 or 9911050030
drvssaxena@gmail.com or sannidhivss@gmail.com

Guidelines for Article Submission to EPILEPSY INDIA NEWSLETTER:

1. **Submission Deadline – ATLEAST ONE month prior** to the month of release of quarterly issue [e.g.- submission for April - June 2018 issue should be by end of March 2018] to avoid carry forward to next quarterly.
2. **Types of articles –**
 - a. **Articles related to epilepsy**
 - b. **Articles** - These can be of scientific &/or general interest, informative, educative to both medical/ non-medical members including persons with epilepsy from disciplines such as - genetics, therapeutics, diagnostics, psychosocial etc
 - c. **Reports on** - chapter activities, CMEs, Conferences **held during the quarter for respective issue that**
 - d. **Awards/achievements** – Please also mail only 1 to 2 relevant photographs
 - e. **Forthcoming events that are planned**
3. **Font type** – Times New Roman **ONLY**
4. **Line spacing** – 1.5
5. **Size of article** – not more than 2- A4 size pages
6. **Ensure corrections to grammar & avoid plagiarism**
7. **Kindly Note** - The newspaper inserts are out of scope of EINL
[suggest you to insert in Chapter newsletter]
8. **References 3-4** – for scientific article must be provided

21st Joint Annual Conference of Indian Epilepsy Association and Indian Epilepsy Society



ECON 2020

17 18 19 JANUARY 2020 | AHMEDABAD

VENUE: Hyatt Regency, Ashram Road, Ahmedabad, Gujarat



PROGRAM HIGHLIGHTS:

1 day workshop on EEG & Imaging in Epilepsy

2 days conference with interactive sessions

Debates & Platform sessions

CPC / Quiz

**Last date of
Abstract
Submission:**
15th
Nov, 2019

REGISTRATION DETAILS:

Category	Upto 31/12/2019	From 01/01/2020	Spot Registration
IEA / IES Members	INR 4,000	INR 5,000	INR 6,000
Non Members	INR 5,000	INR 5,000	INR 6,000
Resident / PG Students	INR 2,500	INR 3,000	INR 6,000
Non Doctor / IEA Members	INR 2,000	INR 2,000	INR 3,000
Accompanying Person	INR 2,000	INR 2,000	INR 3,000
Foreign Delegates	USD 250	USD 300	USD 400
Workshop	INR 2,000	INR 3,000	-----

Registration Fees includes 18% GST

Contact for more information:

Mo.: +91 97262 33228 | Email: econ2020info@gmail.com

Conference Secretariat :

ANSA CLINIC (Advance Neuro Science Associates)

Block M, Mondeal Business Park, Near Gurudwara,

Sarkhej - Gandhinagar Highway, Thaltej,

Ahmedabad, Gujarat 380054

Organizing Chairman

Dr. Sudhir Shah

Organizing Secretary

Dr. Shalin Shah

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WELCOME TO AHMEDABAD, INDIA'S FIRST WORLD HERITAGE CITY

The 606 year old walled city of Ahmedabad, which was founded by emperor Ahmed Shah, has become India's first World Heritage City. The World Heritage Committee (WHC) of UNESCO announced it at Krakwo, Poland.

"For over 600 years, Ahmedabad has stood for peace, as a landmark city where Mahatma Gandhi began India's freedom struggle. It has stood for unity with its elegant carvings in its Hindu and Jain temples as well as standing as one of the finest examples of Indo-Islamic architecture and Hindu Muslim art."

www.econ2020.co.in

ABOUT THE COVER PAGE

PIERRE EYMARD

PIERRE EYMARD the French researcher, fortuitously discovered anticonvulsant activity of Valproic acid in 1962 (VPA; valproate; di-n-propylacetic acid, DPA; 2-propylpentanoic acid, or 2-propylvaleric acid) which was first synthesized in 1882, by Beverly S. Burton as an analog of valeric acid, which is naturally produced by *Valeriana officinalis*. Pierre Eymard while working as a research student at the University of Lyon serendipitously recognized the antiepileptic activity of VPA. Two of Eymard's colleagues, H. Meunier and Y. Meunier, working for a small company, used VPA as a vehicle to dissolve bismuth salt while, testing newly developed compounds for the pentylenetetrazole (PTZ) seizure test and found that VPA exerted anti-convulsant activity. This unexpected finding was first presented at a meeting of the French Society of Therapeutics and Pharmacodynamics on December 19, 1962, and report was published by Eymard along with Meunier, Carraz, Meunier, and Aimard in the French Journal of Therapie in 1963. The French patent (CAM 244) was obtained by Berthier Laboratories in 1969.

The promising data of these preclinical studies led to clinical evaluation of valproate in patients with epilepsy. It was again the group of Carraz which first demonstrated the anticonvulsant effect of valproate in epileptic patients. The results of the earliest clinical trials of the sodium salt of valproate were reported in 1964 by Carraz et al. [7]. Valproate was first marketed for treatment of epilepsy as "Depakine" in France in 1967 (i.e. only 5 years after the discovery of its anticonvulsant activity in rodents) and was commercialized subsequently in more than 100 other countries (in the United States in 1978). Was introduced commercially for use under trade names - Ergenyl, Depakene, Depakane, Depakote, Depakon, Convulex, Epilim, Orfiril, Labazene, Leptilan, Eurekene, and Leptilan.

VPA is now established as a major anti-epileptic drug across the world for various types of epilepsy and is included in the WHO's list of essential medications. Presently, has wide uses in non-epileptic conditions which include - bipolar disorders and migraine. Currently being evaluated for - longer survival in glioblastoma, diabetic peripheral neuropathy and Alzheimer's disease. Its current status is improved by development of new pharmaceutical formulations, such as controlled release or sustained-release formulations, resulting in improved tolerability and reduction in the number of daily intakes. VPA has created a "milestone in drug therapy of epilepsy"!

References:

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