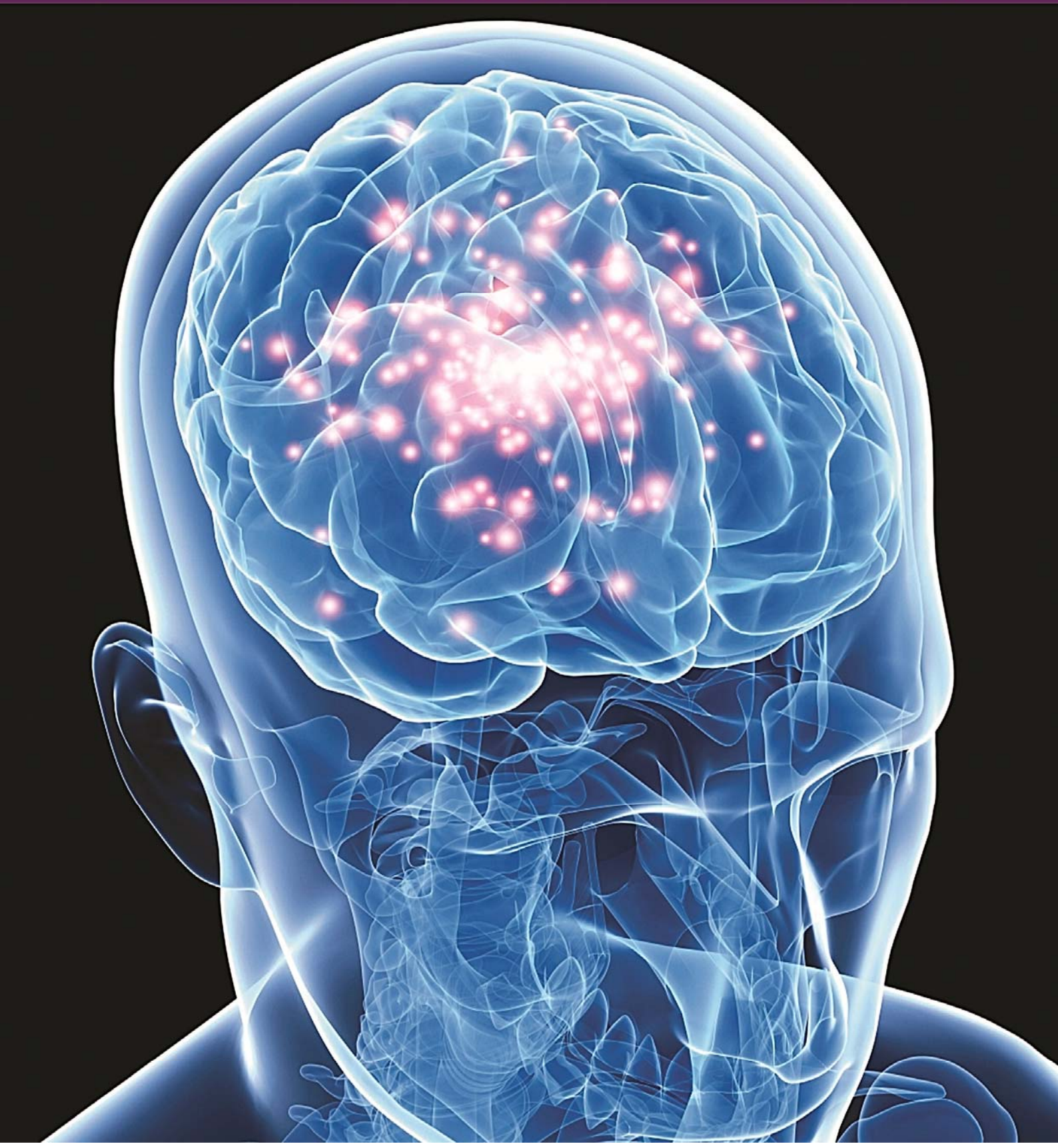
October-December 2017 Issue 4, 2017

Epilepsy India

Newsletter of the Indian Epilepsy Association & Indian Epilepsy Society



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Editorial...

Dr. Bindu Menon

Welcome to last issue of Epilepsy India for the year 2017!

This issue contains an article on 'Epilepsy and Brain tumors'. Seizures can be one of the presenting symptoms of brain tumor and can have a huge impact on the quality of life of these patients. Read an informative article by Dr. Anandh Balasubramanum.

We share with you an interesting epilepsy awareness activity by Uttar Pradesh Chapter as well as an adventurous medical camp conducted at the height of 11,500 feet in Leh. As you continue to read you will have a glimpse of winning accomplishments of our members. Great going indeed for 2017 and we congratulate them. We also hope to and will look forward to receiving many more reports on such exciting events for 2018!!

Dr. Sita Jayalakshmi

Certain rare diseases are chronic and debilitating which can be life threatening. The so-called 'orphan drugs' are intended to treat these rare diseases. Pharmaceutical companies develop such drugs for health needs of these individuals rather than for economic reasons. Dr. Indira Devi, presents a bird's eye view on 'orphan drugs' for epilepsy.

International Epilepsy day 2018 is fast approaching. The International Bureau for Epilepsy [IBE] and the International League Against Epilepsy [ILAE] have announced a photography competition with a theme "Life is beautiful" to mark this day. So, don't forget to pick your camera, to capture life and win prizes!!

Kindly note that a mail has been sent to all the chapters requesting for a mailing list of their current IEA/IES life members. We have received a good response from few chapters; however there are many other chapters yet to respond! We will also appreciate and humbly request all the life members to update their new complete mailing address with us independently when they relocate to receive newsletter on time.

Dr. Chanda Kulkarni

Do continue to contribute articles, stories and share the events on epilepsy with us and we will be glad to include them in our newsletter.

Season's greetings for festivities round the corner and best wishes on behalf of all the members to you and your family for the Year 2018.

EPILEPSY AND BRAIN TUMORS

Dr.Anandh Balasubramaniam
Senior Consultant and HOD, Neurosurgery,
Yashoda Hospital, Secunderabad.

In adults,brain tumors can be a cause of epilepsy. About 35,000 patients per year get diagnosed with brain tumors and more than one third of them develop seizures. If the tumor involves the cerebral hemispheres, seizures occur in at least 50% of cases. (1)

Some predictive factors for seizure occurrence include:tumor location in the frontal or parietal regions, evidence of cerebral hemispheric dysfunction and incomplete tumor resection.
Any brain tumor, benign or malignant, common or uncommon, can cause seizures. Those more highly associated with the development of epilepsy include: melanoma, hemorrhagic lesions, multiple metastases, slowly growing primary tumors and tumors near the Rolandic fissure.

Patients with low-grade tumors may be more likely to develop epilepsy, possibly because their longer survival allows more time for seizures to develop. The tumors most often presenting with seizures in adults are, dysembryoplastic neuroepithelial tumors (DNETs), ganglioglioma, glioblastoma multiforme, low-grade astrocytoma, meningioma, metastatic tumors, oligodendroglioma.

Epilepsy in children is associated with brain tumors less often than in adults. Tumors still must be ruled out, however, even if the child has no neurologic deficits.If a tumor is diagnosed, up to 46% of these patients may have intractable seizures.Most tumors occur in the temporal or frontal lobes. As in adults, epileptogenic brain tumors in children may be benign or malignant. The most common tumors associated with epilepsy in children are, gangliogliomas, low-grade astrocytomas, DNETs, oligodendrogliomas.

Mechanisms of tumor-related epileptogenesis remain poorly understood. In epilepsy associated with tumors, surrounding non tumoral tissue may cause seizures. Abnormal growth kinetics of tumors can affect surrounding neurons morphologically and biochemically, altering neuronal structure and affecting the release of neurotransmitters and neuromodulators such as gamma-aminobutyric acid (GABA) and somatostatin. These changes are likely to cause seizures through either hyperexcitability or reduced inhibition.

The hippocampus may become involved—either directly, through tumor extension, or indirectly, through increased excitatory input caused by a tumor—and may contribute to seizure amplification and propagation. The normal electrical functional patterns of the brain may be disrupted by tumors. This causes increased local coherence. This could be similar to the electrial activity seen electrographically with in cortical region. These are similar to the pattern seen in epileptic foci. These changes, induced by a tumor in the surrounding tissue, contribute to the formation of the epileptogenic zone. Important to resect this zone for treating tumors associated with long term epilepsy. (2)(3).

TREATMENT OF EPILEPSY IN BRAIN TUMOR PATIENTS :

Focal Epilepsy requires focused Treatment.(4)Patients with cerebral neoplasms who develop epilepsy should be treated with antiepileptic drugs (AEDs), but there is no consensus in the literature about which AEDs are

most effective. Studies assessing the use of AEDs in these patients mostly involve the older AEDs, including phenytoin, phenobarbital, carbamazepine, and valproic acid.Where as the newer AEDs, like gabapentin, lamotrigine, tiagabine, levetiracetam, and zonisamide, may offer better efficacy with greater tolerance along with advantage of fewer drug interactions.

DRUG INTERACTIONS

Potential interactions exist between AEDs and medications used intumor therapy. AEDs, such as phenytoin, phenobarbital, and possibly carbamazepine, can induce steroid metabolism due their enzyme inducing properties and thereby decrease its effectiveness. Phenytoin and phenobarbital also may decrease effective concentrations of antineoplastic drugs. One study suggests that phenytoin may have immunosuppressive potential.

Conversely, chemotherapy may alter blood concentrations of AEDs. For example, with Procarbazine therapy increased phenobarbital and phenytoin levels and resultant clinical toxicity can occur. Subtherapeutic AED levels and an increased risk of seizures can develop in patients treated with other chemotherapeutic agents. During concurrent treatment with chemotherapeutic agent's decreased absorption of valproic acid, carbamazepine or increased metabolism of phenytoin may account for these changes. Besides these alterations due to drug interactions or changes in absorption or metabolism, toxicity may occur when AEDs are adjusted in compensation, and a rebound occurs as chemotherapy cycles are concluded.

SIDE EFFECTS

In patients taking AEDs during brain tumor treatment,a variety of adverse side effects have been reported:

- Frequent cutaneous skin reactions, including erythema multiforme and Stevens-Johnson syndrome with phenytoin or carbamazepine in combination with cranial radiation therapy
- Reflex sympathetic dystrophy, affecting the shoulder and hand particularly, usually contralateral to the tumor with phenobarbital
- Agranulocytosis and leukopenia rarely caused by Carbamazepine could complicate use of concomitant che motherapy agents.
- Hepatic toxicity, prolonged bleeding time, and thrombocytopenia with Valproic acid

OTHER PRESCRIBING CONSIDERATIONS

Other AED considerations concern the route of administration, the rapidity of reaching therapeutic levels, and known idiosyncratic and dose- related AED side effects. Medications that are available in intravenous form, such as phenytoin, phenobarbital, leveteracetam and valproic acid, offer an alternative route of administration and can be loaded quickly, allowing for rapid attainment of therapeutic levels, if clinically necessary.

PROPHYLAXIS NECESSARY ?

The need for seizure prophylaxis for patients with brain tumors who have not developed epilepsy is controversial. There has been no significant difference in development of late seizures between patients receiving and not receiving antiepileptic drug (AED) prophylaxis, in most studies. This suggests that AEDs do not revent epileptogenesis. Potential AED side effects and the possibility that patients may remain eizure-free without

treatment may weigh against prophylactic AED therapy. American Academy of Neurology recommends against AED prophylaxis in patients with newly diagnosed brain tumors, in view of its futility.(5)

The evidence regarding perioperative AED prophylaxis is less conclusive. Postoperative seizures occur most often in the first week to first month postsurgery, for patients both with and without tumors.Though many patients with brain tumors receive AED prophylaxis in the perioperative period, there has been no demostrable benefit.Patients with brain tumors are often given prophylactic AEDs to avoid ictal complications in the perioperative period, but there is no controlled evidence that perioperative AED prophylaxis is effective.If patients are treated perioperatively, it is recommended to taper and discontinue the AEDs after the first postoperative week.(6)

WHAT TISSUE SHOULD BE RESECTED ?

Temporal lobectomy is the the most common surgical intervention for intractable complex partial seizures associated with a temporal lobe mass but techniques vary widely between various centres. Some centers advocate the removal of the tumor alone, whereas others stress the importance of resecting the ictal focus, if separate from tumor pathology. Surgery for epilepsy, rather than tumor resection, may be more likely to be considered in those with a longer duration of epilepsy.

Gross total resections are approached with standard craniotomy techniques or via computer-assisted stereotactic cranial procedures. When removal of only the tumor is advocated, gross total resection has been reported as providing greater seizure control than partial resection, with an overall range of 80–88% of patients with temporal or extratemporal lesions achieving complete postoperative relief from seizures.

Conversely, to control seizures it may be necessary to remove epileptogenic cortex beyond the tumor, as has been suggessted by some authors for long. The cortex adjacent to the tumor margins being most likely responsible for epileptogenesis. Seizure relief after resection for the tumor and the epileptogenic zone has been reported as ranging from 80% to 95% for temporal and extratemporal lesions. The surgical strategies have been different varying from resection of epileptogenic cortex to mesial temporal structures resection.(7)

Surgery for oncologic advantages in malignant tumors to prevent tumor spread or progress, along with radiation and or chemotherapy is achived by maximal safe resection principles. The control of seizures in these patients becomes easier with surgical decompression and adjuvant therapy too. (8)

Take home messages :

- Seizure may be an indicator of underlying tumor espcially in adults and should be investigated.
- Tumor with long term seizures may need surgery for epilepsy as they are usually benign and seizures may be intractable. It may require resection of additional epileptogenic zone around the tumor.
- Malignant tumors with seizures need treatment focused on the tumor control and treating the tumor does help in reducing seizures.
- No role for prophylatic seizure medication in brain tumors. Perioperative use is widely practised and AED should be tapered and stopped as soon as possible.
- Newer drugs with less drug interactions and adverse effects with IV administrability may be preferrable. Especially one has to be careful in patients taking chemotherapy and radiotherapy.

REFERENCES :

(1) Van Breemen MSM, Wilms EB, Vecht CJ. Epilepsy in patients with brain tumours: epidemiology, mechanisms, and management. Lancet Neurol 2007; 6: 421–30.

(2) Kohling R, Senner V, Paulus W, Speckmann EJ. Epileptiform activity preferentially arises outside tumor invasion zone in gliomaxenotransplants. Neurobiol Dis 2006; 22: 64–75.

(3) Baayen JC, de Jongh A, Stam CJ, de Munck JC, Jonkman JJ, Trenité DG, et al. Localization of slow wave activity in patients with tumorassociated epilepsy. Brain Topogr 2003; 16: 85–93.

(4) Marjolein de Groot; Jaap C. Reijneveld; EleonoraAronica; Jan J. HeimansBrain. 2012; 135(4):1002-1016.

(5) Glantz MJ, Cole BF, Forsyth PA, et al. Practice parameter: Anticonvulsant prophylaxis in patient with newly diagnosed brain tumors. Neurology 2000; 54:1886–1893.

(6) Mangano FT, McBride AE, and Schneider SJ. Brain tumors and epilepsy. In: Ettinger AB and Devinsky O, eds. Managing epilepsy and co-existing disorders. Boston: Butterworth-Heinemann; 2002; 175–194.

(7) Sanai N, Berger MS. Glioma extent of resection and its impact on patient outcome. Neurosurgery 2008; 62: 753–64.

(8) Epilepsy in Patients With a Brain Tumour. Focal Epilepsy Requires Focused Treatment.Marjolein de Groot; Jaap C. Reijneveld; EleonoraAronica; Jan J. HeimansBrain. 2012; 135(4):1002-1016.

Reported by :
DR. ATUL AGARWAL
Secretary IEA UP Chapter

The Department of Pharmacology, Hind Institute of Medical Sciences, Barabanki successfully organized the above CME. Prof JV Singh, Principal of the medical school inaugurated the CME. Dr Atul Agarwal, spoke about current therapeutic status of anticonvulsant medications in clinical practice. Dr Vimlesh Verma discussed the problems encountered in chronic dosing with anticonvulsants. Dr Utkarsh Bansal elaborated on management of paediatric convulsions. The organising secretary, Dr A K Khare discussed the usefulness of therapeutic drug monitoring of anticonvulsant medications. Dr Rekha Khare highlighted on Neurocysticercosis, as the leading and preventable cause of secondary epilepsy. The CME was attended by large number of faculty members, interns and medical students of the institute.

The department also conducted a free Epilepsy camp at an altitude of 11,500 feet in Leh (Laddakh) on 8th& 9th June with the help of local NGO, Mr Motup and his team. The camp was well attended since the patients were pre registered for the free camp. Dr Atul Agarwal evaluated 98 patients with Epilepsy and 72 other patients with neurological problems. Dr Sangeeta Agarwal delivered an awareness lecture on epilepsy to a large group of children. The team distributed free anticonvulsant medications to patients with epilepsy who attended the free camp.

A public awareness lecture on Epilepsy and Stroke was organized at the auditorium of Hindustan Aeronautics Ltd (HAL), facilitated by Dr Surabhi. Mr Rajiv Kumar, CEO, HAL, organized these lectures for HAL employees. Lecture was delivered by Dr Atul Agarwal, who explained all aspects of epilepsy, including management and myths associated with epilepsy. The program was well appreciated and was followed by long question answer session. Dr Pankaj Kumar was the master of ceremony.


People
With
Epilepsy:
Thanks for your kind attention

Dr Parthasarthy Satishchandra received the Ambassador for Epilepsy Award at the 32nd International Congress on Epilepsy [IEC] in Barcelona, Spain held between September 2-6, 2017. The Ambassador for Epilepsy Award is intended as recognition of outstanding international contributions to activities advancing the cause of epilepsy, either internationally or with an international impact. The award is given biannually at the IEC.

Dr. (Professor) Man Mohan Mehndiratta has been elected member of Commission on Asian and Oceanian Affairs (ILAE) for a period of 4 years and Vice Chair- South East Asia (IBE)

Sheryl Haut, Tina Budnitz, Bindu Menon, Param Kharbanda, Jaideep Kapur

Reported by
Dr Param S. Kharbanda.
Professor of Neurology,
Postgraduate Institute of Medical Education & Research (PGIMER).

I had the privilege of participating in the ILAE/IBE leadership program conducted at Barcelona, September 2nd – 3rd 2017, during the International Epilepsy Congress. Bindu Menon, myself, and delegates from other countries, were a part of this half-day program, which focused on honoring the leadership skills of people involved in planning comprehensive epilepsy care. It was a well crafted program with a good mixture of lectures delivered by stalwarts - Dan Lowenstein , Solomon Moshe, Ingrid Scheffer, Helen Cross, Michael Privatera , Emilio Perucca , Sam Wiebe in the field of epilepsy and Tim Keogh in leadership development. This was followed by interactive discussions and goal generation exercises. The agenda encompassed topics involving general leadership skills and styles to issues more focused on Epilepsy. Held together by Jaideep Kapur and Sheryl Haut, and anchored by Tina Budnitz , on behalf of ILAE. The course also had lectures on conflict resolution, financial planning, strategic planning, scientific communication and future vision. It was a great opportunity to meet and interact with the members of Management Committee of ILAE & IBE, and the other leaders and past alumni of the leadership course. Dr Bindu and me would like to thank the IEA and IES for supporting our nomination for leadership program, and will forward to using this enriching experience to contribute to the local and global epilepsy initiatives.

Dr.C. Indira Devi
Rtd.Addl.Director, Director of Medical Education

Orphan drugs in Epilepsy

Childhood epilepsy differs in their expression and treatment response. Several childhood epilepsy syndromes affect cognition and development due to the effect of persistent electrical activity on the immature brain.Treatment in this group of children is not only aimed at preventing seizures, but also at abolishing ictal and interictal EEG abnormalities. In this context some drugs called orphan drugs have been designated for some of the childhood epilepsy syndromes with grave prognosis.

An **orphan drug** is developed to treat a rare medical disease, which is itself called an orphan disease. These diseases affect a small minority of population and are genetic in majority of cases. The assignment of orphan status to the disease and the developed drugs is a medical breakthrough with issue of public policy too. The Orphan drug act was passed in 1983 to establish incentives to drug companies to develop treatments for rare diseases. In 2016 only 5% of all the orphan drugs were for neurological disorders. In neurological disorders neuro degeneration and epilepsy are the common indications for the Orphan drug approval. Epilepsy syndromes predominated by seizures, cognitive and motor problems are the most targeted group for the **orphan drug space.**

Orphan drugs for epilepsy are Vigabatrin, Adrenocorticotropic hormone and corticosteroids, Stiripentol, Felbamate, Rufinamide.

Vigabatrin is a GABA –transaminase inhibitor is one of the first- choice agent for infantile spasms.Severe neonatal epileptic encephalopathies may respond to vigabatrin. (1)Side effects of Vigabatrin are drowsiness, agitation, excitement, insomnia, behavioral difficulties, vision disturbances such as blurring or double vision and allergic reaction.

Stiripentol was designated as an orphan drug for the adjunctive treatment of Dravet syndrome (severe myoclonic epilepsy in infancy. It elevates the levels of gamma-aminobutyric acid (GABA). Common adverse effects include gastrointestinal symptoms, reversible neutropenia, insomnia, drowsiness, aggression and irritability. (2)

Rufinamide is a fast sodium channel blocker has been approved for the treatment of seizures associated with Lennox-Gastaut syndrome in children four years and older and adults. Common adverse reactions are headache, dizziness, fatigue, somnolence and nausea.

Adrenocorticotropic hormone (ATH) and corticosteroids - ACTH is a 39-amino acid polypeptide secreted from the anterior pituitary. ACTH has been used since the last 20 years for the treatment of West syndrome. Side effects include hypertension, recurrent infections, weight gain, behavioral problems,

Felbamate was designated an orphan drug status in 1993 - Felbamate potentiates GABA function, blocks

voltage-dependent sodium channels and NMDA antagonist. Felbamate potentiates gamma aminobutyricacid (GABA) function, and as well as the ionic channel at the N-methyl-D-aspartate excitatory amino acid receptor in vitro.Felbamate is indicated in refractory Lennox-Gastaut syndrome. Common side effects are headache, rash, aplastic anemia and liver failure.(3)

REFERENCES :

1) Baxter PS, Gardner-Medwin D, Barwick DD, Ince P, Livingston J, Murdoch-Eaton D.Vigabatrinmonotherapy in resistant neonatal seizures.Seizure. 1995 ;4(1):57-9.

2) Brigo, F; Igwe, SC; Bragazzi, NL. "Antiepileptic drugs for the treatment of infants with severe my oclonic epilepsy.". The Cochrane database of systematic reviews. 5: CD010483.(18 May 2017).

3) Rho JM, Donevan SD, Rogawski MA. "Barbiturate-Like Actions of the PropanediolDicarbamates Felbamate and Meprobamate". J. Pharmacol. Exp. Ther. 1997; 280 (3): 1383–91.

Photography competition to celebrate International Epilepsy Day 2018

To celebrate International Epilepsy Day 2018, we are delighted to announce an international photography competition for all ages with the theme 'Life is Beautiful'. We are keeping the theme deliberately wide, to allow competitors to choose how they would like to reflect the theme - that life is beautiful despite a diagnosis of epilepsy; that life is beautiful when enjoyed with family and friends; or that nature shows us how beautiful life is!

There shall be two categories – under 12 years of age and over 12 years of age and the competition is open to everyone!

All entries shall be placed in a gallery on the International Epilepsy Day website epilepsy.org.

PRIZES

The competition prize fund is US$2,000, as follows:

Under 12 years

- 1st Prize of US$500
- 5 runners up prizes of US$100 each

Over 12 years

- 1st Prize of US$500
- 5 runners up prizes of US$100 each

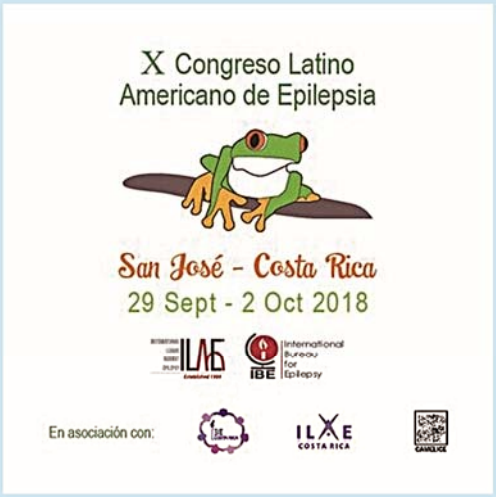
COMPETITION RULES

- Photos should reflect the theme 'Life is Beautiful'.
- Photos must be submitted by email to ibeexecdir@eircom.net.
- Photos should be a minimum of 1MB and a maximum of 6MB preferably 300dpi (in particular for photos taken using regular cameras).
- Photos may be taken using a regular camera, smartphone or tablet.
- Entrants must provide their name, address, age (if under 12 years) and email address.
- Each entry must be entirely the original work of the contestant, must have a title (in English) and indicate the location in which the photo was taken.
- Any person included in a photo must have given their express permission to be photographed.
- By submitting a photograph to IBE the contestant agrees to grant IBE, free of charge, the right to publish the photograph online and in other IBE media.
- Closing deadline for entries is 31st December 2017 and all entries must be submitted electronically.
- The winning entry shall be announced on International Epilepsy Day – 12th February 2018.
- Entrants under 16 years of age, must obtain your parent's or guardian's permission before entering the competition.
- There is no limit on the number of entries a contestant may submit.
- The judges' decision is final and no correspondence shall be entered into.
- IBE reserves the right to disqualify any entry which breaches any of these rules.
- An independent judging panel, to be announced shortly, shall select the winners and runners up.

REMEMBER THE CLOSING DATE IS 31st DECEMBER 2017!

12th Asian and Oceanian Epilepsy Congress
28 June - 1 July 2018
Bali, Indonesia

13th European Congress on Epileptology
26 - 30 August 2018
Vienna, Austria



10th Latin American Congress on Epilepsy
29 September - 2 October 2018
San José, Costa Rica

This biennial meeting, which is a joint collaboration of the International Bureau for Epilepsy (IBE) and the International League Against Epilepsy (ILAE) in association with the IBE Chapter in Costa Rica, the Costa Rican Chapter of the International League Against Epilepsy and the Mexican Chapter of the International League Against Epilepsy (CAMELICE), which provides a unique opportunity to meet with the experts in the epilepsy field.

33rd International Epilepsy Congress

22 - 26 June 2019
Bangkok, Thailand