AAN EPILEPSY THERAPY UPDATE

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Introduction
The armamentarium of Epilepsy therapies has increased in the last several years in the major therapeutic categories of medicines, devices and epilepsy surgery. The newest available epilepsy therapies should be considered in patients with hard to control or refractory epilepsy. Newly available and effective therapy allows the practitioner expanded treatment options that can be customized to maximize outcomes and minimize suffering.

Medication Developments
60% of patients will respond to the first line appropriately selected anti-epileptic drug (AED) (Kwan and Brodie, 2000). Unfortunately, 30 to 40% of PWE are not adequately controlled after two adequate trails of medication. When these first two AEDs have failed the PWE have a less than 10% probability of achieving seizure freedom additional medication trials (Kwan and Brodie 2000). The International League Against Epilepsy (ILAE) has defined drug resistant epilepsy as "failure of adequate trials of two tolerated, appropriately chosen and used AEDs to achieve sustained seizure freedom". (Kwan et al, 2010). This is a VERY important concept to consider when dealing with hard to control seizures. It is recommended that people with medically refractory epilepsy should be referred to a comprehensive epilepsy program for surgical consideration or other non-medication therapies (Fountain et al, 2015).

Newer medications available in the USA offer options to offer the person with epilepsy. Several unique medications are now available that can be added to existing regimens or by themselves. The following drugs in Table #1 have been approved by the USFDA. Make note of Parampanel, Lacosamide, Brevitriacitam (See-Talk), Vigabatrin, and Ezlicarbazipine (talk).

Surgical Developments
Epilepsy surgery is a therapeutic option for patients with disabling, medically intractable focal epilepsy. The most commonly performed epilepsy surgery is temporal lobectomy. In a landmark trial of Best medical management vs. temporal lobectomy, the superiority of surgery over medical management has been proven in a randomized trial, Outcome measures for seizure control, mortality, and quality of life were all reported to be better. (Wiebe et al., 2001). Post temporal lobectomy, 65% of patients are seizure free at 5 years, and another 20% have improved seizure control. Best outcomes are seen in the subset of patients with mesial temporal sclerosis, with seizure free rates after surgery approaching 80%. For patients with neocortical epilepsy, seizure free rates following focal cortical resections about 50% become seizure free overall. It should be noted that with better outcomes are seen well defined lesions on MRI. The rate of major complication is only 1-2% for experienced surgical programs.

Stereo EEG: Although not technically a therapy, the potential promise of the so called "stereo EEG" may be used to as a localization tool. This technique is touted to more precisely localize the ictal onset zone prior to resective surgery for focal epilepsy, especially in non-lesional cases of PWE. This may have the potential to produce better outcomes post resection. The technique involves insertion of multiple depth electrodes stereotactically inserted in the region of the suspected ictal onset zone. The technique is generally better tolerated than large numbers of grids and standard electrodes and requires methodical planning and special expertise. (Koubiessi,Bancoud,Cossu)

Laser Ablation: Standard temporal resection and lesionectomy typically requires a craniotomy and resection of large amounts of brain tissue. The downside of classical epilepsy resection typically includes a fairly lengthy recovery time. In selected cases, with smaller lesions or precise ictal onset zone, laser ablation can be considered in many circumstances. Typical locations range from the hypothalamus to doing a truly selective amygdalohippocampectomy. (Wicks)

Devises and palliative procedures for refractory Epilepsy: When resective surgery is not a reasonable option, due to the underlying epilepsy syndrome, inability to safely resect or precisely localize the ictal onset zone or even patient choice. Other so-called palliative procedures such as multiple subpial transection (MST), hemispherectomy, corpus callosotomy, vagus nerve stimulation (VNS), or implanting an responsive

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neurostimulator (RNS) device (Morrell) may be potential options of the person with MRE. Dietary therapies such as ketogenic diet or the modified Atkins diet are not new, their use has shown renewed interest in challenging cases. To be successfully used dietary therapy can be considered in motivated adults and children.

Complementary and Alternative Medicine (CAM)

Medical Marijuana, Marijuana and Derivatives.
The whole topic of Marijuana is not technically NEW; renewed interest has definitely exploded in this area. This has occurred even in the "popular press" as evidenced by the Iconic report on a young girl in Colorado with Dravet's syndrome finding dramatic improvement in her seizures using CBD oil. The use of Marijuana and its derivatives remains controversial for widespread usage; the appropriate and interested organizations have position statements on the matter and will be explored in the presentation. Several formalized drug studies are finally underway. (*https://www.youtube.com/watch?v=oxrKyjeCITk; CNN Gupta, accessed 2/27/2017); (Ref: 18)*

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Table 1. Anti-Epileptic Drugs: Indications and Side Effects (modified K Noe MD PhD)

Drug	FDA Labeled Indication	Common Side Effects	Severe Idiosyncratic Reactions	
Carbamazepine	Partial Epilepsy	Dizziness, ataxia, nausea, fatigue, diplopia	Rash, hyponatremia, hepatotoxicity, pancreatitis, bone marrow suppression	
Clobazam	LGS	Sedation, aggression	Rash	
Eslicarbazepine	Partial Epilepsy	Nausea, dizziness, headache, sedation	Hyponatremia, transaminitis, rash	
Ethosuximide	Absence	Nausea, headache, dizziness, ataxia	Rash, bone marrow suppression	
Ezogabine	Partial epilepsy (intractable)	Dizziness, tremor, fatigue	Urinary retention, psychosis, blue skin pigmentation, retinal disorder/vision loss	
Felbamate	Partial Epilepsy (intractable), LGS	Weight loss/anorexia, headache, insomnia	Fulminant hepatic failure, aplastic anemia	
Gabapentin	Partial Epilepsy	Sedation, weight gain, edema		
Lacosamide	Partial Epilepsy	Nausea, headache, dizziness	Cardiac arrhythmia	
Lamotrigine	Partial and Generalized Epilepsy, LGS	Headache, nausea, dizziness, diplopia	Rash	
Levetiracetam	Partial and Generalized Epilepsy, Myoclonic Seizures	Depression, irritability, insomnia		
Oxcarbazepine	Partial Epilepsy	Nausea, headache, dizziness, ataxia	Rash, hyponatremia	
Perampanel	Partial epilepsy, GTC seizures	Dizziness, headache, somnolence	Severe mood disturbance – homicidal ideation, rash	
Phenobarbital	Partial Epilepsy, GTC Seizures	Sedation, cognitive impairment, hyperactivity,	Rash, hepatotoxicity, anemia	
Phenytoin	Partial Epilepsy, GTC Seizures	Ataxia, dizziness, nausea, headache, gingival hyperplasia	Rash, hepatotoxicity, bone marrow suppression	
Pregabalin	Partial Epilepsy	Weight gain, edema		
Rufinamide	LGS	Nausea/vomiting, headache, dizziness, fatigue	Rash, Shortened QT interval, status epilepticus, leukopenia	
Tiagabine	Partial Epilepsy	Tremor, nausea, cognitive impairment, fatigue	Non-convulsive status epilepticus	
Topiramate	Partial and Generalized Epilepsy, LGS	Fatigue, cognitive slowing, aphasia, anorexia, weight loss, paraesthesia	Nephrolithiasis, acute angle closure glaucoma, metabolic acidosis, hyperammonemia	
Valproate	Partial and Generalized Epilepsy	Weight gain, tremor, nausea, menstrual disorders, hair loss, sedation	Rash, hepatotoxicity, pancreatitis, hyperammonemia, thrombocytopenia	
Vigabatrin	Partial Epilepsy (intractable), Infantile Spasms	Weight gain, tremor, nausea, dizziness, headache, somnolence	Irreversible vision loss, rash, hepatotoxicity	
Zonisamide	Partial Epilepsy	Anorexia, dizziness	Rash, nephrolithiasis, metabolic acidosis, aplastic anemia	

Abbreviations: FDA = United States Food and Drug Administration, LGS = Lennox Gastaut Syndrome, GTC = generalized tonic clonic

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