# Medications for Epilepsy – What I Need to Know

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# **Learning Objectives**

- Treatment options for seizures
- What factors affect which medication is prescribed for you?
- Common side effects of medications
- Drug interactions
- Monitoring of medications
- Medication adherence



# **Seizures and Epilepsy**

#### Seizure

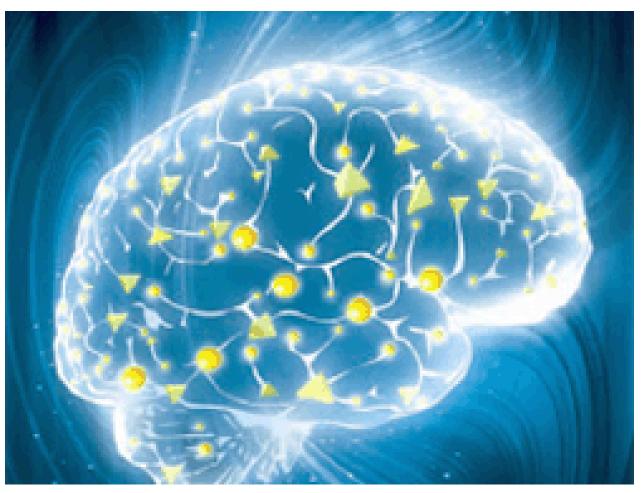
Abnormal electrical activity in brain cells

#### Epilepsy Recurrent unprovoked seizures





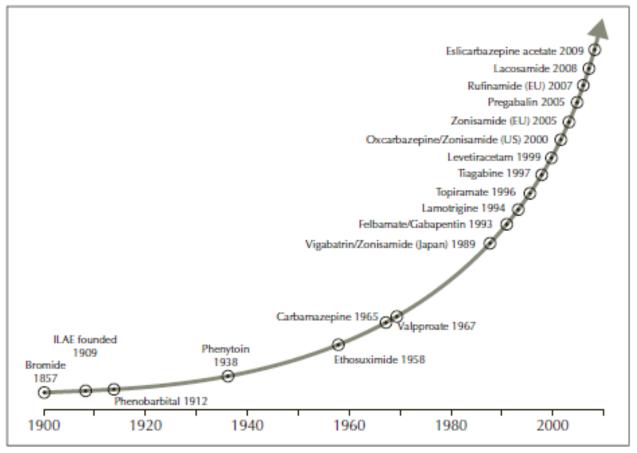
#### **Anti-Seizure Medications**



Narasimhan, K. Zooming in on Seizures, Nature Neuroscience, 15 (179) 2012.



# Anti-Seizure Medications Past and Present



Arzimanoglou et al. The evolution of antiepileptic drug development and regulation, Epileptic Disord 2010; 12 (1): 3-15



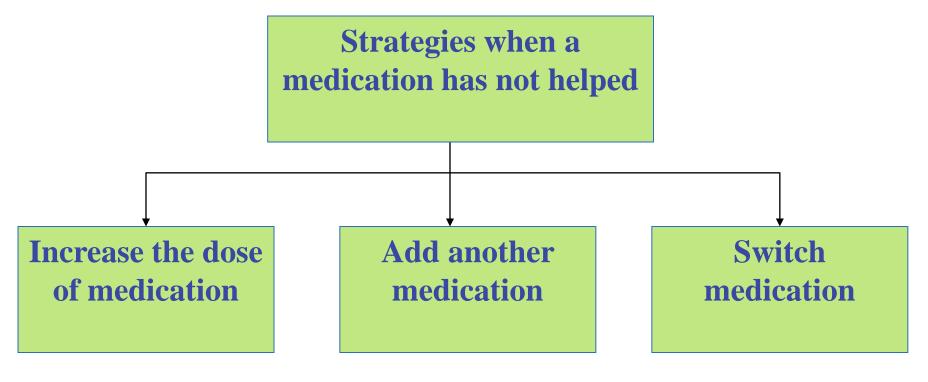
#### **Anti-Seizure Medications The Future**

- Gap needs to be filled to find treatment options for refractory patients
- Research is being done to:
  - Find new drugs with novel chemical structures, new targets and different mechanisms of action
  - To understand how epilepsy occurs
     Look for disease modifying agents
     Look for genetic biomarkers that can identify people at risk of developing epilepsy



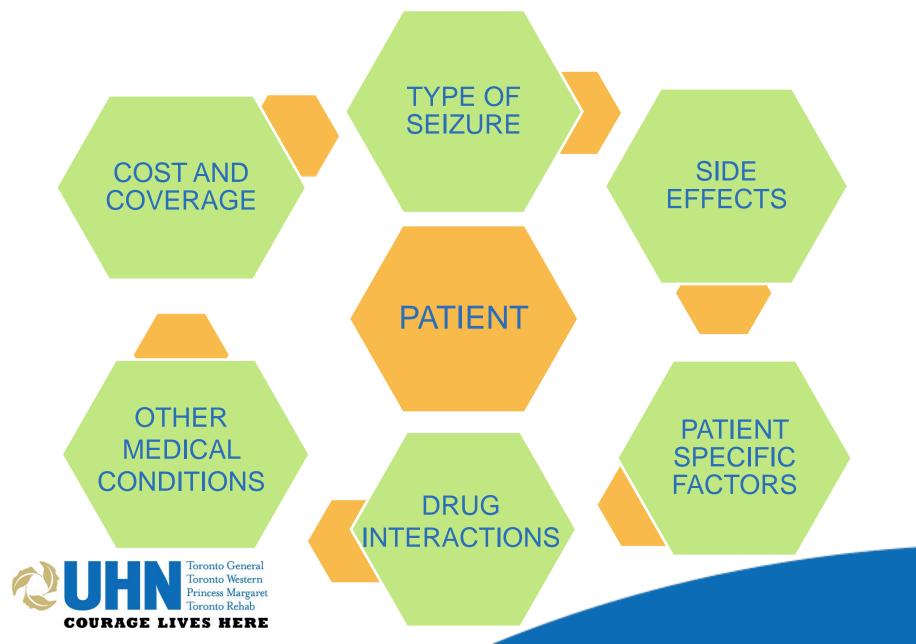
#### **Anti-seizure Medications continued**

50-70% of patients respond to one medication





#### **How are Medications Selected?**



# **Type of Seizure**

- Seizures can be divided into two main categories
  - Generalized seizures
  - Focal seizures
- Some medications tend to work better for certain types of seizures than others



#### **Type of Seizure**

#### **Generalized Seizures**

#### **Focal Seizures**

- Valproic acid / Divalproex sodium (Epival)
- Phenytoin (Dilantin)
- Carbamazepine (Tegretol)
- Oxcarbazepine (Trileptal)
- Topiramate (Topamax)
- Lamotrigine (Lamictal)
- Levetiracetam (Keppra)
- Clonazepam
- Ethosuximide (Zarontin)
- Rufinamide (Banzel)

- Carbamazepine (Tegretol)
- Phenytoin (Dilantin)
- Valproic acid / Divalproex sodium (Epival)
- Phenobarbital
- Primidone
- Oxcarbazepine (Trileptal)
- Topiramate (Topamax)
- Lamotrigine (Lamictal)
- Levetiracetam (Keppra)
- Clobazam
- Gabapentin (Neurontin)
- Pregabalin (Lyrica)
- Vigabatrin (Sabril)
- Lacosamide (Vimpat)
- Perampanel (Fycompa)
- Eslicarbazepne (Aptiom)



## Side Effects

Medication side effects

How well medication works



## **Patient Specific Factors - Women**

- Some medications may be avoided because of their side effect profile
- Certain medications may be preferred for women of child-bearing age
- During pregnancy, seizure frequency can change
  - Decrease in seizure threshold
  - Decrease in medication concentrations



## Patient Specific Factors - Women Birth Defects

- Increased rate of birth defects in children of mothers with epilepsy
- Seizures can be harmful to mother and fetus
- Higher risk in the 1st trimester
- Tips when considering pregnancy:
  - Plan ahead and see your Neurologist early
  - Ensure you are taking folic acid and prenatal vitamins



## **Patient Specific Factors- Elderly**

- May be on multiple medications for other conditions that can interact
- May be more at risk of having side effects
- Tips for managing medications:
  - Tell Doctors and Pharmacists about all new medications
  - Doctor may make dose adjustments more slowly
  - Pay attention to how you feel after any changes have been made

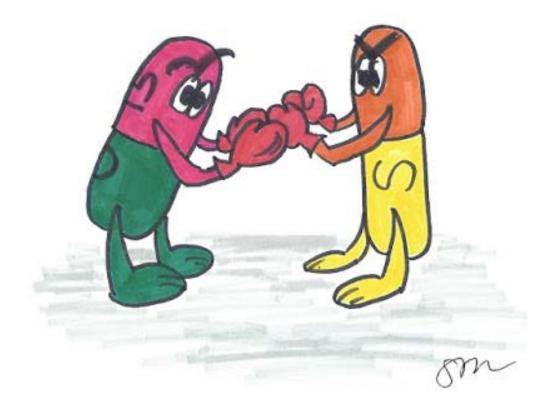


#### **Patient Specific Factors -What has Worked in the Past**

- Helpful to know which medications have been trialed in the past
  - What has worked
  - What was not helpful or not tolerated
- Tips for managing medications:
  - Keep a log of medications you have been on (dates and response)
  - Keep a list of medications you have reacted to or not tolerated well



## **Drug Interactions**



http://www.medicineslearningportal.org/2015/07/interactions-introduction.html



#### **Other Medical Conditions**

Seizure medications can be useful for other conditions

Condition	Anti-seizure Drug of Choice
Trigeminal neuralgia	Gabapentin, pregabalin, carbamazepine
Bipolar disorder	Lamotrigine, valproic acid
Migraine	Topiramate, valproic acid
Neuropathic pain	Gabapentin, pregabalin
Fibromyalgia	Pregabalin



# **Cost and Coverage**

- Some medications can have higher costs
- Private insurance companies usually cover most medications
- Government programs
  - Ontario Drug Benefit Program (ODB)
  - Trillium Drug Program



## SIDE EFFECTS OF MEDICATIONS





## **One Pair Does Not Fit All**



http://www.elle.com/fashion/trend-reports/news/g18326/falls-best-jeans/



## **Dose Related Side Effects**

Side Effect	Drug
Double vision, feeling unsteady, dizziness, feeling tired	Most medications
Irritability	Levetiracetam (Keppra)
Word-finding difficulty	Topiramate (Topamax)
Tremor	Valproic acid / Divalproex sodium (Epival)



## **Long-term Side Effects**

Side Effect	Drug
Cosmetic changes	Phenytoin (Dilantin)
Decreased bone mineral density	Phenytoin, phenobarbital, carbamazepine, valproic acid
Kidney stones	Topiramate (Topamax)
Difficulty with vision	Vigabatrin (Sabril)
Weight loss	Topiramate (Topamax)
Weight gain	Valproic acid, carbamazepine, gabapentin, pregabalin, vigabatrin





#### **Rash related to Anti-seizure Medications**

• Can occur in medications with similar chemical structure:

Phenytoin (Dilantin)	Carbamazepine (Tegretol)
Phenobarbital	Lamotrigine (Lamictal)
Oxcarbazepine (Trileptal)	Primidone

- Usually happens within the first 2 months of starting the medication
- Can become a serious reaction that affects internal organs
- Must seek medical attention



#### **Rash related to Anti-seizure Medications**

#### **Treatment**

- Discontinue offending anti-seizure medication
- Switch to alternate agent
- Treat the symptoms
  - > Antihistamines
  - Steroids may be necessary





#### **DRUG INTERACTIONS**





# **Drug Interactions**

- Many anti-seizure medications can interfere with
  - > Other medications for epilepsy
  - Drugs for other conditions
- This can lead to higher or lower drug concentrations in the body



## **Some Common Drug Interactions**

- Oral Contraceptives
- Blood thinners
- Cholesterol Lowering Medications
- Heart medications
- Antidepressants
- Antibiotics
- Antiviral medications
- Anticancer medication
- Herbals/Natural Products



# **Drug Interactions**

#### **Tips for managing drug interactions:**

- Ensure all Doctors and Pharmacists know the medications you are taking
   Including non-prescription medications
- Have medications filled at one pharmacy
- Keep notes on:
  - > Any change to seizure type or frequency
  - > Any new side effects



## MONITORING OF MEDICATION LEVELS





# **Drug Monitoring**

- Blood tests can be done to check levels of certain medications
- Some common examples:

Phenytoin (Dilantin)	Valproic acid / Divalproex sodium (Epival)
Carbamazepine (Tegretol)	Phenobarbital



# **Drug Monitoring**

- Levels may be checked when:
  - Starting a new medication
  - Changing medication dose
  - Possible drug interaction
- Levels are usually drawn prior to dose
- Doses may not always be changed based on levels alone



#### **MEDICATION ADHERENCE**







- For medications to help prevent seizures, there needs to be a consistent amount in the body
  - Take medications regularly
  - Do not miss doses
- Tips to help remember medications
  - Request blister packs from pharmacy
  - Set alarm on clock
  - Smartphone App to track medications



# Non-Pharmacological Options

- Avoid triggers
- Maintain seizure and side effect diary
- Dietary changes (useful in some children)
- Surgery (for treatment resistant patients that are appropriate candidates)





- Seizure treatment options have increased in recent years and more research is in progress
- Many factors are considered when selecting a medication for each patient
- Monitor for side effects when starting new medications
- Many anti-seizure medications can interact with other drugs
- Blood tests can be done for some medications
- Medication adherence is important for seizure control



## **Useful Websites**

**Epilepsy Toronto** 

http://epilepsytoronto.org/

**Canadian Epilepsy Alliance** 

http://epilepsymatters.com/

Epilepsy Foundation http://www.epilepsy.com/









#### References

Arzimanoglou, A.et al. The evolution of antiepileptic drug development and regulation, Epileptic Disord 2010; 12 (1): 3-15

Brodie, M., Antiepileptic drug therapy the story so far, Seizure 19 (2010) 650–655

Brodie, M., Sills, G. Combining antiepileptic drugs - rational polytherapy?, Seizure 20 (2011) 369-375

Johannessen, SI. Can Pharmacokinetic Variability be Controlled for the Patient's Benefit? The Place of TDM for New AEDs. Therapeutic Drug Monitoring, 2005: 27(6): 710-713

Johannessen, SI, Tomson, T. Pharmacokinetic Variability of Newer Antiepileptic Drugs. Clin Pharmacokinetics, 2006: 45(11): 1061-1075 Johannessen, SI. et al. Therapeutic Drug Monitoring of the Newer Antiepileptic Drugs. Therapeutic Drug Monitoring, 2003: 25: 347-363 Klein, AM. Epilepsy Cases in Pregnant and Postpartum Women: A Practical Approach. Seminars in Neurology, 2011: 31 (4): 392-396 Knowles SR, et al. Expert Opin Drug Safety 2012; 11:767-78

Koda-Kimble, M. et al. Applied Therapeutics – The Clinical Use of Drugs. 8th Edition, Baltimore: Lippincott Williams & Wilkins, 2005: 54-1 – 54-42

Kwan, P. et al. Drug Resistant Epilepsy. New England Journal of Medicine, 2011;365:919-926

Lexi-Comp Online, Lexi-Drugs Online, Hudson, Ohio: Lexi-Comp, Inc.; 2013

Micromedex® 2.0 Healthcare Series. n.d. Thomson Healthcare, Greenwood Village, CO. 2013

Nadkarni, S. et al. Current Treatments of Epilepsy. Neurology, 2005;64(Suppl 3):S2-S11

Narasimhan, K. Zooming in on Seizures, Nature Neuroscience, 15 (179) 2012

Patsalos, P. Clinically relevant drug interactions with antiepileptic drugs, Epilepsia 43(4): 365-385, 2002

Perucca, E. An Introduction to Antiepileptic Drugs. Epilepsia, 2005: 46(Suppl.4): 31-37

Perucca, E., Tomson, T. The Pharmacological Treatment of Epilepsy in Adults. Lancet Neurology, 2011: 10: 446-456

Perucca, P, Gilliam, F. Adverse Effects of Antiepileptic Drugs. Lancet neurology, 2012: 11: 792-802

Perucca, E. Clinically relevant drug interactions with antiepileptic drugs, Br J Clin Pharmacol. 2006 Mar; 61(3): 246–255

Sander, J.W., The Natural History of Epilepsy in the Era of New Antiepileptic Drugs and Surgical Treatment, *Epilepsia*, 44(Suppl. 1):17–20, 2003

St. Louis, EK. Minimizing AED Adverse Effects: Improving Quality of Life in the Interictal State in Epilepsy Care, *Current Neuropharmacology*, 2009, *7*, 106-114

Suppes, T., Majares, K. Dosing and Monitoring Guidelines for Anticonvulsants. Primary Psychiatry, 2004: 11(10): 53-70 Thundiyil JG, et al. J Med Toxicol 2007;3:15-19

Thomson, AH. Introduction to Clinical Pharmacokinetics. Paediatric and Perinatal Drug Thearpy, 2000: 4(1): 3-11 Tomson, T., Battino, D. Teratogenic Effects of Antiepileptic Drugs. Lancet Neurology, 2012: 11: 803-813





