



Do we have a plan for breakthrough seizures?


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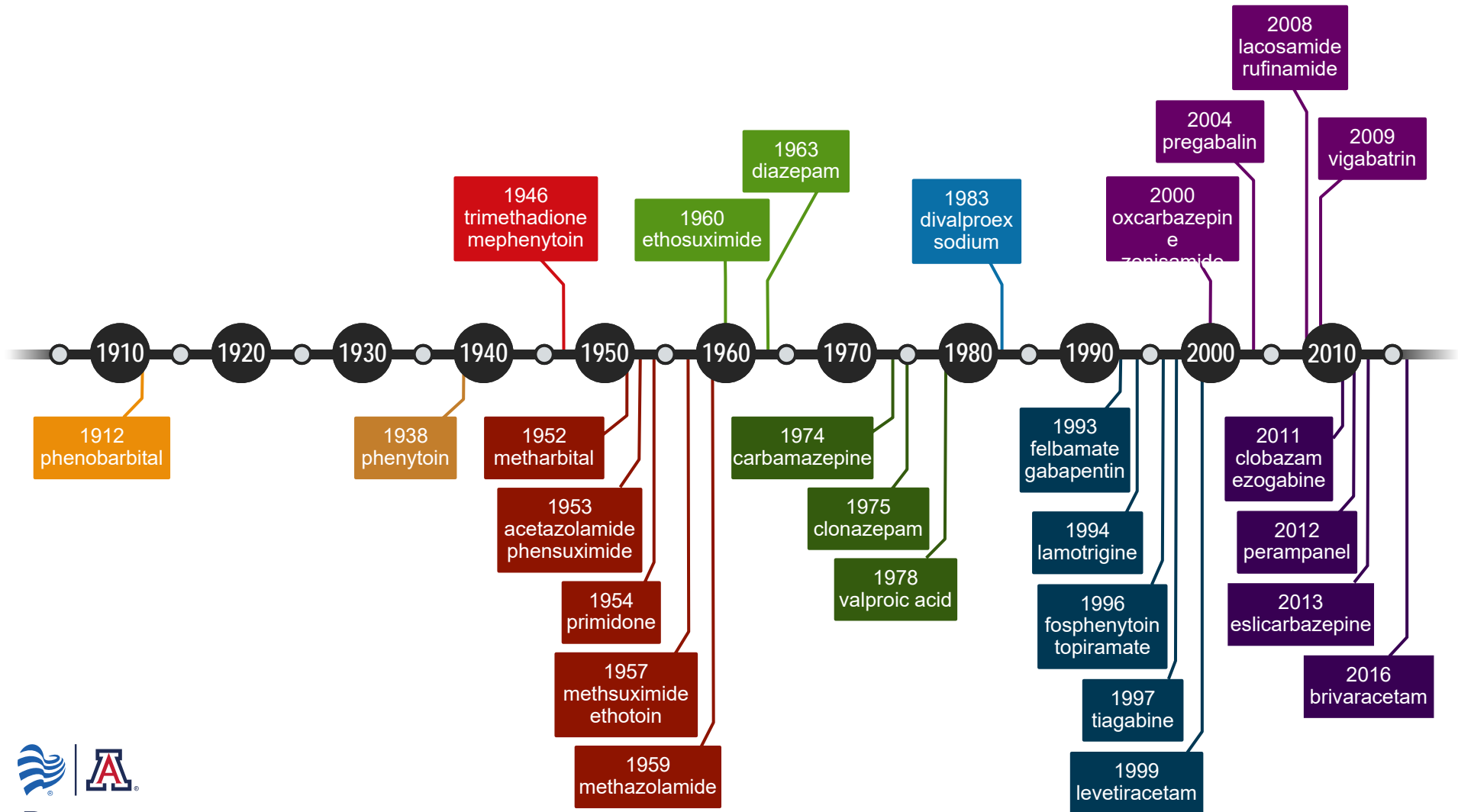


What do you do when breakthrough seizure happens?

1. Call 911
2. Call the doctor's office
3. Call friends and family for help
4. Take an extra pill
5. Take a rescue medication



So many medications





What are we missing?

- For most of AEDs initial approval is limited to focal epilepsy
- No clear guideline which medications should be used for individual patient case (Clinical study is based on population study)
- One significant unmet needs in epilepsy care:
RESCUE MEDICATIONS



Characterizing Seizure Clusters

- Seizure clusters can be broadly defined as acute episodes of consecutive seizures that occur with short interictal periods and may be distinguishable from a patient's typical seizure pattern or frequency

Alternative Names for Seizure Clusters

Acute Repetitive Seizures	Recurrent Seizures	Flurries
Crescendo Seizures	Serial Seizures	Cyclical Seizures

Patients who experience seizure clusters represent ~15% of the uncontrolled epilepsy population and ~5% of the total epilepsy population, or **about 150K to 200K patients in the United States**





Definition of Seizure Cluster

- Even though there is no consensus, SC can be defined clinically (most commonly ≥ 3 seizures in 24 h)
- More than usual seizure frequency





When do we need rescue Med?

- Seizure clusters
- Prolonged seizures
- Pre-status state
- While traveling
- During AED transition



Serious Consequences with Seizure Clusters

Physical injury

~30% of patients report bodily injury linked to seizures, such as head trauma, burns/scalds, dental injury, and fracture, with seizure type, severity, and frequency being key predictors of risk

Hospitalization

Seizure clusters have been linked with a high rate (73%) of emergency-related hospitalization

Status epilepticus

Occurs 3.5 times more often in clustering patients than in patients who do not have clusters (44% vs 12.5%, respectively)

Neurological damage

Repetitive seizures have been associated with long-term cortical brain damage and cognitive decline

Mortality

The risk of death is 3.49 (95% CI, 1.25-9.78) times greater than in the general epilepsy population



Seizure Emergency Action Plans

259 patient survey reports:



Clinician Recommendations

	Patients (N=259)	Clinicians (N=339)
Rescue medication	20%	79%
Call doctor's office	20%	67%
Visit ER	24%	61%
Stay calm	34%	50%
Extra/increased dose of AED	11%	28%
VNS	10%	21%
Visit urgent care	7%	12%
Other	5%	2%
Typically nothing	27%	1%



Penovich PE, et al. *Neurologist*. 2017;22:207-214.

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What we have now

- Rectal Diazepam (Diastat) 1997
- Intranasal Midazolam (Nayzilam) 2019
- Intranasal Diazepam (Valtoco) 2020



Rectal Diazepam (Diastat)



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Nasal Midazolam (Nayzilam)



Nasal Diazepam (Valtoco)



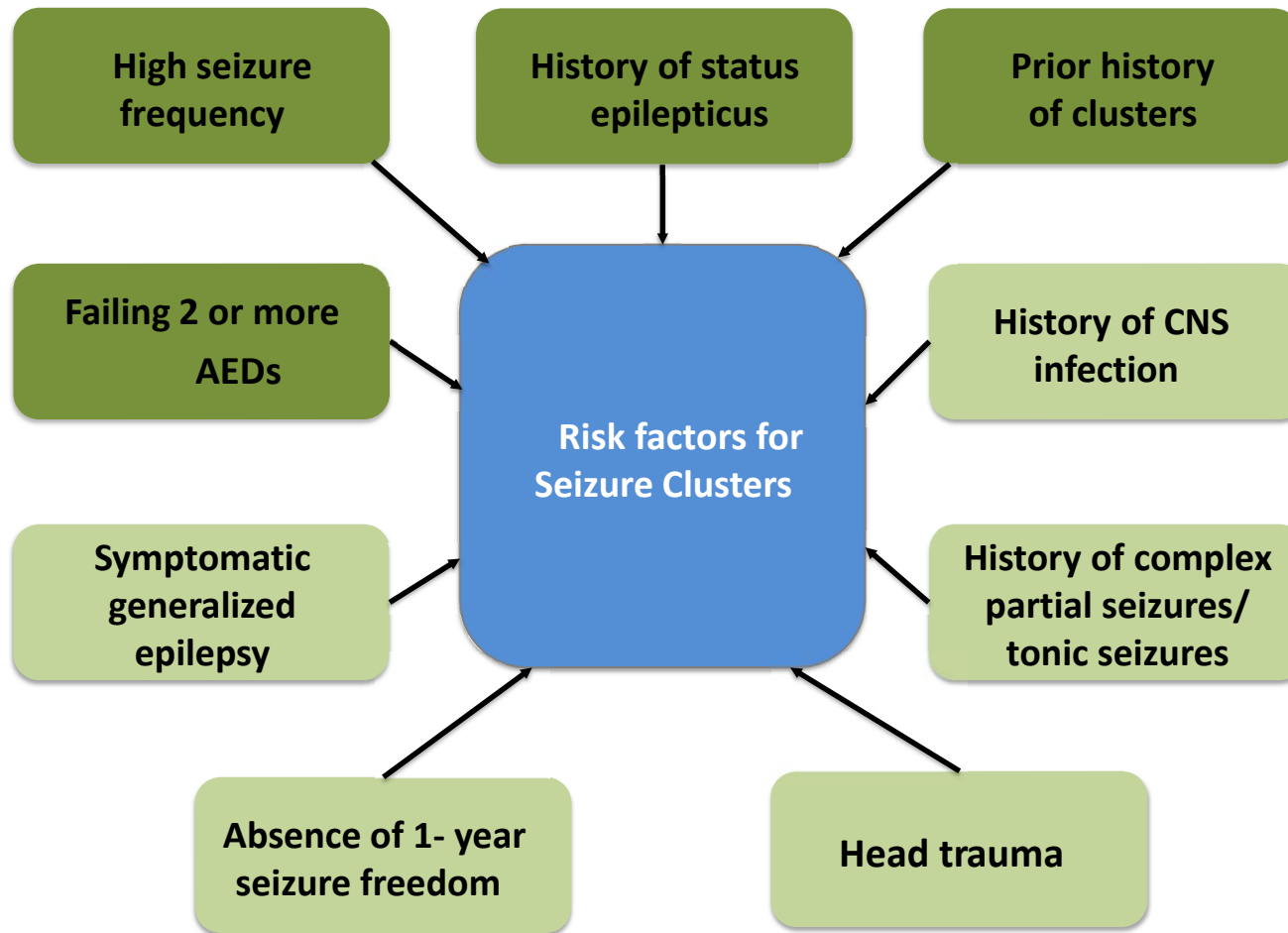


What we will have

- Intrabuccal Diazepam film
- Inhaled Alprazolam



More severe seizures = Seizure cluster more likely

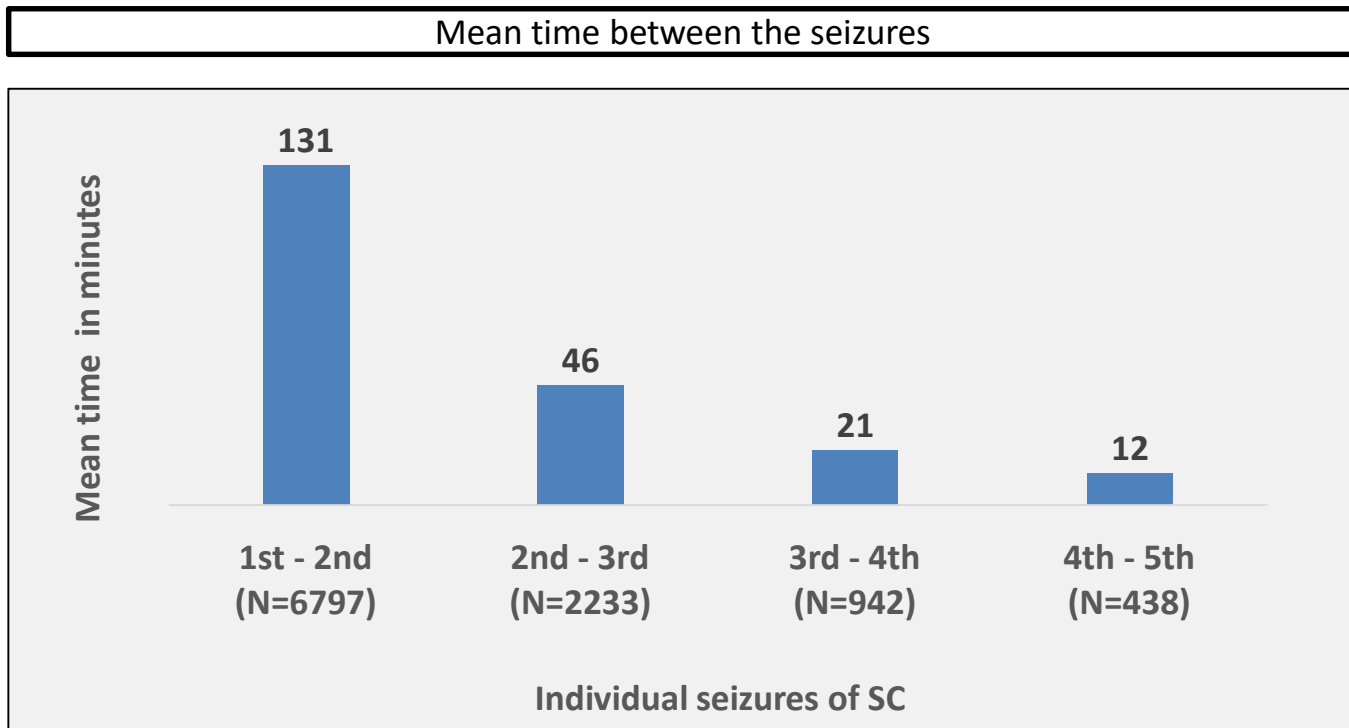


- Other *possible* risk factors include:
 - Younger age at epilepsy onset
 - Extra-temporal localization
 - Cortical dysplasia
 - Remote symptomatic epilepsy
- For the above mentioned risk factors, inconsistent evidence of association was reported in the literature



-] Adequate data and consistent evidence of association (≥ 2 studies)
-] Limited data for evidence of association (1 study)

The mean time between seizures decreased with more seizures and time



- 1,177 SC patients of multiple seizures in a 24-hour period
- Among days with at least 2 seizures, **one-third** of the seizures occurred **within 3h** and two-thirds within 6h of each other





Preferred Rescue Medication?

- Quick Onset
 - Fast penetration through BBB
 - Minimal delay in dosing
- Fast Functional Recovery
 - Short half life, short drowsiness
- Portability, Convenience
- Broad Spectrum for all kinds of seizures
- Long shelf life





Let's have a plan together!

- Patients and patient's family should be clear about what to do when breakthrough seizure occur, under the doctor's guidance.



Questions?



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