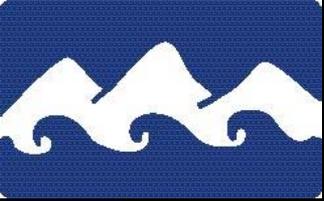


Initial Treatment of Seizures in Childhood

Roderic L. Smith, MD, Ph.D.

Pediatric Neurology Clinic of
Alaska, PC



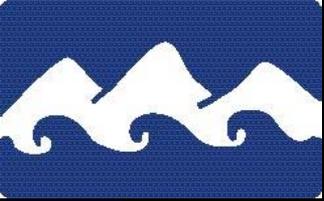
Incidence of Seizures

Overall 5% by age 20 yrs.

Lifetime risk= 5-10%

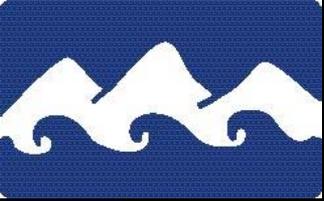
CNS Infections= 5%

TBI=10%



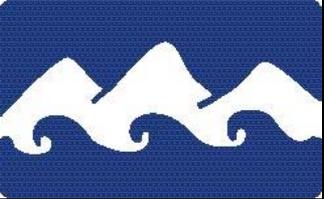
Incidence of epilepsy

- Bimodal peak of epilepsy
 - ◆ Infancy and childhood, elderly
 - ◆ Lifetime risk 3-5%
 - ◆ Prevalence 1%



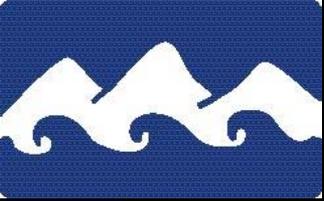
To treat or to wait on therapy

- *Straightforward to wait*
 - ◆ Rare febrile seizures
 - ◆ Syncopal convulsions
 - ◆ First time unprovoked seizure



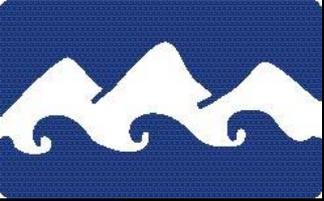
To treat or to wait on therapy

- *Complex decision making*
 - ◆ Recurrent benign seizures (e.g., Benign Rolandic, infrequent absence, complex febrile)
 - ◆ Second seizure
 - ◆ First seizure with a known abnormal EEG or a condition with increased risk (CP, tumor, old injury)



To treat or to wait on therapy

- *Straight forward to threat*
 - ◆ Threatening presentations (status epilepticus)
 - ◆ Serious co-morbidities; infection, stroke, tumor, trauma with hemorrhage



Treatment Options

- Treatment is tied directly to:
 - ◆ Underlying cause
 - ◆ Risk/benefit of medications
 - ★ Side effects
 - ★ Recurrence risk
 - ★ Safety, compliance, access to care
 - ★ Incomplete safety and efficacy data in childhood



Classification of Seizures-Generalized

Absence

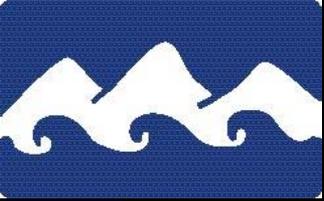
Myoclonic

Tonic

Clonic

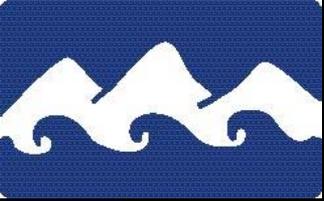
Tonic-clonic

Atonic



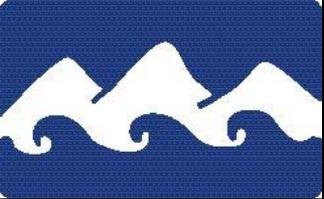
Classification II

- 2. Partial/Focal
 - ◆ Simple
 - ◆ Complex
 - ◆ With secondary generalization



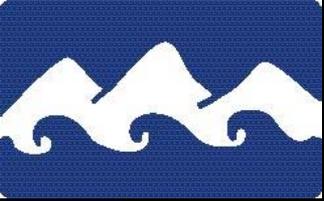
Classification III

- Unclassified seizures
 - ◆ Febrile
 - ◆ Neonatal
 - ◆ Reflex
 - ◆ Nonepileptic
 - ◆ Acquired Aphasia



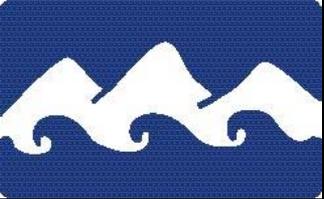
General Approaches to seizures

- No treatment for first seizure
- Hx, PE, directed further evaluation.
- EEG any first afebrile seizure.
- Imaging of brain in selected situations
- Treat for 2nd, or 3rd seizure: excepting status, febrile seizures.
- Initial drug-
 - ◆ Infant—Phenobarbital
 - ◆ Child/toddler— levetiracetam or Tegretol/Trileptal if EEG normal. VPA, levetiracetam, Lamictal or Zonegran if spike and wave.
 - ◆ Diastat for first aid



Status epilepticus—in the field

- Supportive (airway, glucose, etc.)
- Use of benzodiazepines, rectal valium (Diastat) up to 0.6 mg/ kg, up to 20 mg size. Some caution in children under 2 yrs old at high doses.
- Intravenous diazepam or lorazepam



Status epilepticus in hospital

Stop seizures!

- ◆ Benzodiazepines

- ★ Ativan 0.1mg/kg

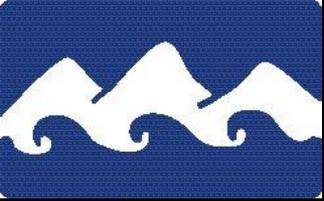
- ★ Phenobarbital 20 mg/kg

- ★ Fosphenytoin 20 mg/kg (PE)

- ★ May repeat either phenobarbital or phenytoin 10 mg/kg

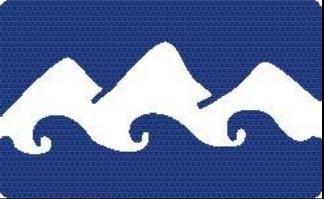
(IV levetiracetem may replace phenobarbital)

- Hx, PE, Labs (Lytes, Ca, Mg, Glucose, tox),
- Imaging, EEG



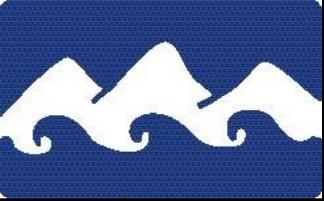
Refractory Status (>60 min)

- Grave situation
- Requires specialized ICU care



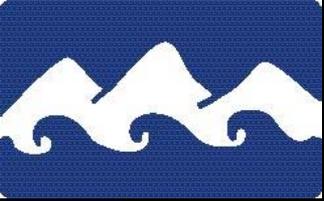
Neonatal seizures

- Etiology usually clear or strongly suspect
- HIE
- Subarachnoid hemorrhage
- Drug withdrawal-opiates, SSRIs
- Infection
- Stroke, venous thrombosis
- Severe electrolyte disturbance
- Metabolic-Urea cycle, glycine encephalopathy, pyrodoxine dependency, proprionic, methylmalonic, Mo cofactor deficiency, etc.
- Benign familial neonatal epilepsy



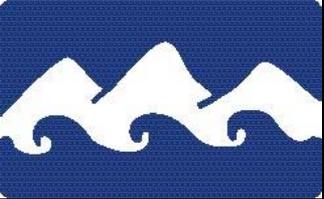
Neonatal seizures

- Multiple types: focal, tonic, clonic, multifocal, subtle.
- Clinical: grimace, focal change in tone, clonic movements, bicycle, lip-smacking, eye deviation.
- Apnea is a unique and threatening form of seizure in term infants.



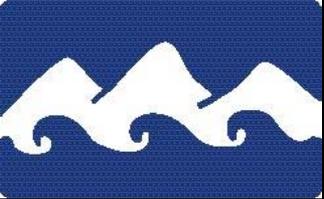
Treatment

- Treating the underlying problems may be critical to outcome.
- Increasing evidence for seizures contributing to outcome.
- Unique problem of life-threatening apnea with seizures of even a benign cause.



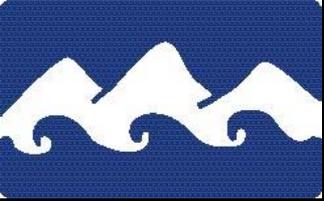
Evaluation

- Hx, PE, Labs (Lytes, Ca, Mg, Glucose), imaging, EEG
- Stop seizure-
 - ◆ Benzodiazepines
 - ★ Ativan 0.1 mg/kg (NO DIAZEPAM)
 - ★ Phenobarbital 20 mg/kg
 - ★ Fosphenytoin 20 mg/kg (PE)
 - ★ May repeat either phenobarbital or phenytoin 10 mg/kg



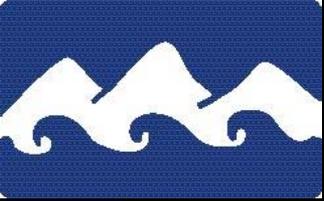
Additional AEDs?

- Increasing movement of very aggressive seizure management
- Special cases-Pyridoxine and other metabolic disorders
- Keppra and Zonegran, Topamax also in use. Tegretol/Trileptal is occasionally used requiring high doses of meds. All these are off-label, but widely used measures.



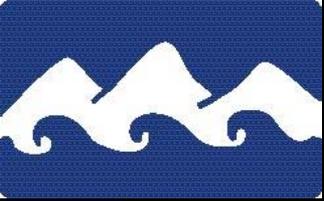
Prognosis

- Determined by underlying cause
- Infant with normal exam has 90% chance of no further seizures, and normal development.
- Even in infants with significant issues, stroke, HIE therapy may be short term-weeks to months depending on local approaches



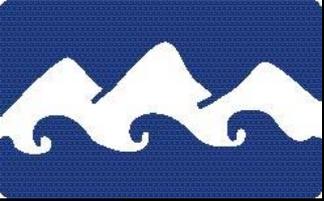
Febrile seizures

- Most common cause of childhood epilepsy—linked to 2 major Na⁺ channel mutations. Usually occurs later than 3 months and ends by 4 years.
- Many other seizure types may be activated by fever.
- History (with family history), exam, routine laboratory, consideration of cause of fever, and presence of a normal interictal EEG are diagnostic. Gene testing is available, but not recommended.



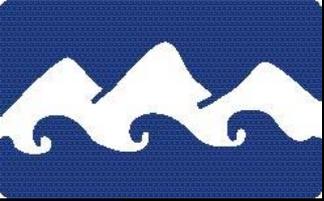
Treatment of febrile seizures

- If seizure is prolonged, can treat as any case of status epilepticus with a higher preference for phenobarbital.
- Phenobarbital (and valproate) can reduce risk of recurrence but are not recommended except in rare situations.
- Rectal valium has been the treatment standard



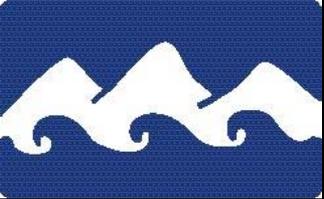
Febrile Status epilepticus

- Usually occurs early in the course of febrile seizures and can be focal.
- Most common cause of status epilepticus with an unusually favorable prognosis for this diagnosis.
- Most studies are moving away from daily preventive seizure medications.



Syncopal convulsions

- Common with breath holding spells.
- Relatively common in adolescence and adult life.
- Rarely associated with long seizures, and treatment-resistant at all ages.



Absence vs Daydreamer

Absence

-3-12 yrs.

Peak 6-8 yrs.

Girls >Boys

A few to Hundreds
a day

Interrupts speech,
activity

Hyperventilation
provokes absence

GTC 40%

Remit usually 10-
11

- 10% refractory

Daydreaming,
ADD

Same age

Boredom

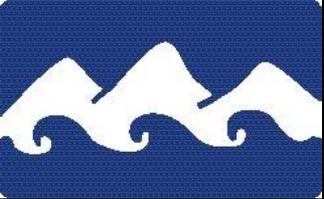
Less frequent

Longer duration

Will not interrupt

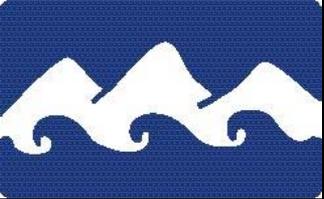
Hyperventilation
will not provoke

Many children with
absence also
have ADD



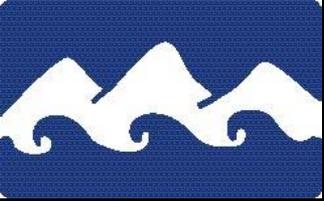
Treating Absence

- Ethosuximide vs. Valproate
- Ethosuximide and valproate are used at 10-40 mg/kg divided bid to tid. Use extended release form of valproate if possible.
- Both require monitoring laboratories
- Carbamazepine, oxcarbazepine, phenytoin contraindicated



Treatment refractory absence

- 10-15% of cases.
- Higher risk in younger (3-4 yr old) or older (>10 yr)
- Often require multiple medications in combination. Little science to support choices.
- Keppra, Zonegran, Topiramate are possible adjunctive agents. No proof of effectiveness.



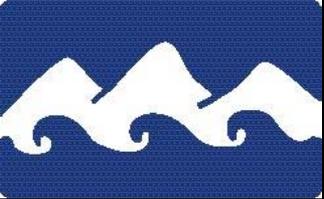
Special forms of absence

- For atypical cases (Juvenile absence or adolescent females, Lamotrigine is usually preferred (3-6 mg/kg divided bid)
- “Spike wave stupor” rare presentation of a “stuck” absence seizure—benzodiazepine or valproate effective



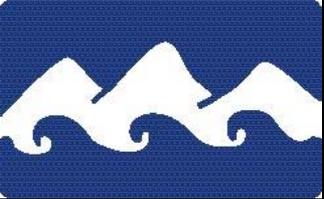
Benign Rolandic seizures

- Responsive to gabapentin, topiramate, lamotrigine, levetiracetam, oxcarbazepine. Oxcarbazepine is probably drug of choice, if decision to treat is made.
- Expanding number of nocturnal seizure syndromes, but most are variants of Rolandic seizures.



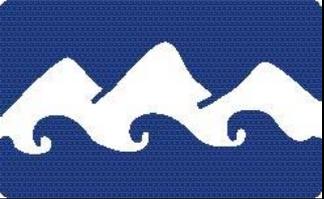
Benign Rolandic Seizures + other localization epilepsies

- Carbamazepine/ oxcarbazepine
- Important exception-nocturnal seizures with occipital spikes do best with valproate.
- Nocturnal symptomatic complex partial seizures are common
- A variety of less common focal seizures occur.



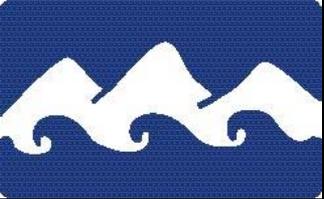
Juvenile Myoclonic Epilepsy

- Common generalized epilepsy-10% childhood
- GTC anytime, may precede other finding which is
- Myoclonus upon awakening-mistaken for clumsiness, tremor or shakes.
- Onset 12-18 yrs.
- EEG with polyspike and wave 4-6 Hz. (1/3 normal EEG, 1/3 3 Hz spike and wave)
- Atypical absence 30%
- Myoclonus is exacerbated by sleep deprivation, EtOH.
- Life long disorder (women often outgrow in 20's)



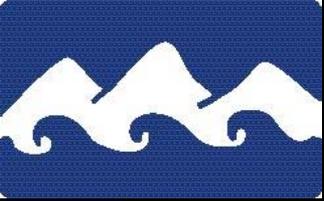
Treatment of JME

- Issues of polycystic ovary disease and significant weight gain with VPA.
- Many advocate lamotrigine as first line agent with consideration of zonisamide, levetiracetam
- Increasing focus on life-style modification.



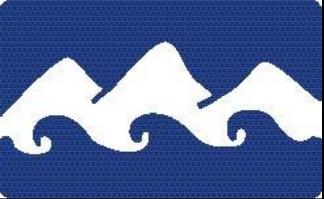
Myoclonic Epilepsies

- Includes brief myoclonic seizures with “drop attacks”
- Often associated with developmental delay
- Treatment involves specialized decision making, but benzodiazepines or valproate can be used.
- Best to collaborate with neurology in decision making.



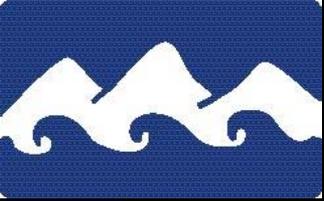
Infantile Spasm

- Initial treatment consist entirely of correctly recognizing the condition.



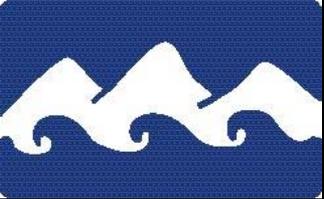
Infantile spasm

- 4-8 months
- 90% present by one year of age
- Characterized by seizure type, age of onset, EEG (hypsarrhythmia)
- Flexion, extension or both
- 40% no cause found (cryptogenic)
- Recognition of motor behavior is role of initial treatment. W/U and treatment is specialized.
- Primary care has a special role in supporting treatments.
- Treat-ACTH, vigabatrin



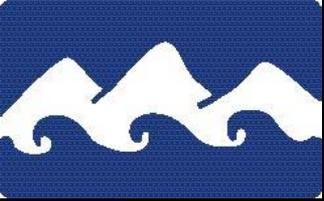
Treatment of infantile spasm

- Vigabatrin not yet FDA-approved (on Fast-track)
- Usual dose is 80-100 mg/kg/day
- 10-30% risk of visual field restriction.



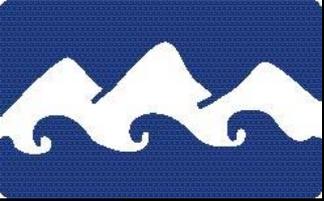
Treatment of infantile spasms

- Consensus that ACTH should be attempted in all other cases.
- Debate on dose remains unresolved, but higher doses and shorter duration is the present trend.
- Cost is a major issue >\$10,000-30,000/wk



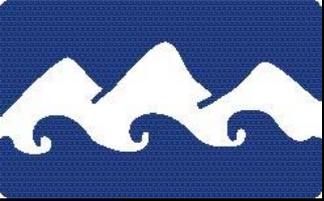
Discontinuing meds.

- Risk of recurrence-
 - ◆ Overall 30-50%
 - ◆ Risk factors-
 - ★ EEG findings
 - 27% if normal
 - 44% if abnormal
 - ★ Etiology
 - Symptomatic(known cause-HIE, trauma, etc.) - 68%
 - Idiopathic- - 37%



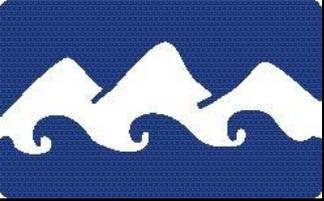
Recurrence

- Recurrence
 - ◆ Sleep state with seizure
 - ★ Asleep-53%
 - ★ Waking-36%



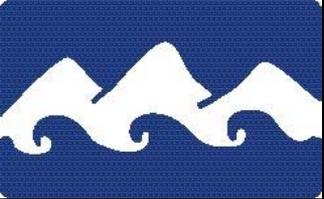
Recurrence, etc..

- NOT predictive of recurrence:
 - ◆ Duration of seizure
 - ◆ Family Hx
 - ◆ Status Epilepticus, but recurrence may be prolonged if occurs.
 - ◆ ?Treatment
 - ◆ Age?, less than 2, focal motor.



Withdrawal of Medication

- 2 years seizure-free in US (Europe after 1 year).
- Risk of recurrence-25 to 40%
- Most recur within 6 mos. 80% by one year.
- Increased risk?
 - ◆ Abnormal exam, EEG
 - ◆ Increasing age of onset.
 - ◆ ? Seizure type

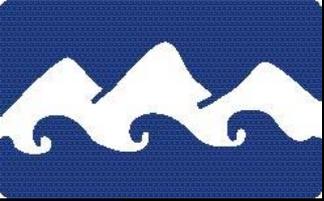


Young women and Epilepsy

- Teratogenic effects of Valproate- (need for high dose folate)
- Teratogenic effects of new generation drugs is unknown, but appear favorable.
- Issues of effects on oral contraceptive agents—
- Issues of bone demineralization

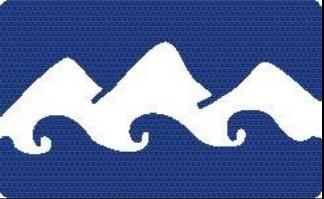


- “It is vain to do with more what can be done with fewer.
--William of Occam



Appendix

- Specific drugs follow in a set of slides describing some specifics of dose.
- Slides that follow are included for reference



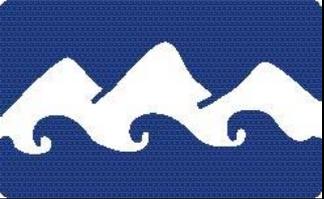
“New” treatment options

- Useful reformulation and derivative of medications
- “New” agents
 - ◆ Lamictal (lamotrigine)
 - ◆ Topamax (topiramate)
 - ◆ Zonegran (zonisamide)
 - ◆ Keppra (levetiracetem)
 - ◆ Gabitril (tiagabine)
 - ◆ Trileptal (oxcarbazepine)



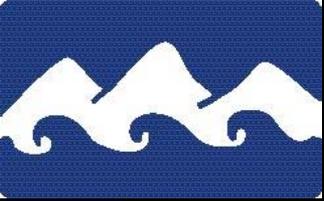
Topamax (topiramate) Zonegran (zonisamide)

- Broadly effective, can be used in young children according to experience.
- Side-effects similar; related to carbonic anhydrase effects; renal caculi, narrow angle glaucoma, poor tolerance of high temperature.
- Topamx has special cognitive concerns.
- Zonegran has some sulfa like structural characteristics.
- Probable bone demineralization—risk for virtually all anticonvulsants.



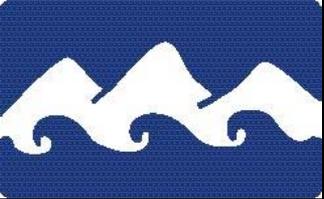
Dosage and formulation

- Topamax and Zonegran: available as sprinkle caps
- Topamax: dosing 2-8mg/kg/day
- Zonegran: water soluble and stable
 - ◆ 7-20 mg/kg/day—once a day dosing possible



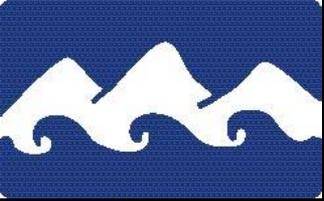
Trileptal

- Dosing is 50-200% greater than Tegretol.
- Available as liquid
- Usually a single set of electrolytes obtained 2-3 months after starting



Trileptal (oxcarbazepine)

- Activated form of carbamazepine—avoids hepatic and bone marrow effects.
- Still can change renal H₂O clearance and produce hyponatremia—mostly an issue of hot climates and athletics.
- Must request specific levels
- Bone demineralization; probably better than carbamazepine
- Improvement for Alaskan patients because of drug monitoring.
- Note much higher dosing recommendations since release.



Keppra (levetiracetem)

- Broadly effective.
- Few serious side-effects, no need for blood monitoring.
- May cause severe agitation in some youngsters
- Commonly used in combination with Zonegran for myoclonic seizures.
- Effective in partial seizures
- Extensive use outside of approved ages
- Recent evidence suggest role in tic disorders—not approved or confirmed



Adjunctive therapies in refractory seizures

- Evaluation for epilepsy surgery
- Ketogenic diet—
- Vagal nerve stimulator--
Adjustments can be made by any
local provider.