Seizure Disorders Update

Nurse Practitioner, Certified Nurse-Midwives and Physician Assistant Continuing Education

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Learning Objectives

• Recognize the clinical features of seizures
• Compare & contrast various seizure types including adult vs. pediatric seizures
• Describe/perform a comprehensive neuro exam
• Discuss critical decision-making in the medical evaluation of suspected seizure
• Review the treatment & management of seizures
• Describe the considerations in special populations such as pregnancy
Definition

• Seizure - behavior that occurs when the brain has *abnormal rhythmical electrical discharge*

  – Manifested clinically by an impairment or loss of consciousness, abnormal motor activity, sensory disturbances, behavioral and emotional abnormalities, or autonomic dysfunction.

• Epilepsy - *recurrent* tendency to have seizures *without* provocation

Epidemiology of Epilepsy

• Third most common neurological disorder in the United States after Alzheimer’s disease and stroke.

• Not a single entity but a family of more than 40 syndromes that affects >3 million people in the U. S. and 50,000,000 worldwide.

• Most often strikes the very young and the very old, although anyone can get it at any age.

• Annual economic burden of $15.5 billion on the nation in associated health care costs, losses in employment, wages and productivity.

• The mortality rate among people with epilepsy is 2-3X higher than the general population; the risk of sudden death is 24 times greater.
Organization of epileptic conditions

### Table 14.1: Schema for Organizing Epileptic Conditions

<table>
<thead>
<tr>
<th>With Generalized Seizures</th>
<th>With Partial (Focal) Seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary (idiopathic) epilepsies</strong></td>
<td></td>
</tr>
<tr>
<td>Without structural lesions; benign; genetic</td>
<td>Absence (petit mal) epilepsy</td>
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<tr>
<td></td>
<td>Juvenile absence epilepsy</td>
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<tr>
<td></td>
<td>Many generalized tonic-clonic seizures</td>
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<tr>
<td></td>
<td>Juvenile myoclonic epilepsy</td>
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<tr>
<td></td>
<td>Benign neonatal seizures</td>
</tr>
<tr>
<td><strong>Secondary (symptomatic) epilepsies</strong></td>
<td></td>
</tr>
<tr>
<td>With anatomic or known biochemical lesions</td>
<td>Infantile spasm</td>
</tr>
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<td></td>
<td>Lennox-Gastaut syndrome</td>
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<tr>
<td><strong>Conditions with reactive seizures</strong></td>
<td></td>
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<tr>
<td>Abnormal reaction of an otherwise normal brain to physiologic stress or transient epileptogenic insult</td>
<td>Febrile seizures</td>
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<tr>
<td></td>
<td>Most toxic and metabolic induced seizures</td>
</tr>
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<td></td>
<td>Many isolated tonic-clonic seizures</td>
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<td></td>
<td>Early post-traumatic seizures</td>
</tr>
</tbody>
</table>


Classification & Terminology

International Classification of Epileptic Seizure (1981)

- still most widely used
- constantly being modified
- many new schemes have been proposed

### Table 14.2: Classification of Epileptic Seizures

I. Partial (focal or local) seizures
   - Simple partial seizures
   - Seizures with motor signs
   - Seizures with somatosensory or special sensory symptoms
   - Seizures with autonomic symptoms or signs
   - Seizures with psychic symptoms
   - Complex partial (psychomotor) seizures
   - Simple partial (focal) seizures evolving to secondary generalized (tonic-clonic, grand mal) seizures
   - Complex partial (psychomotor) seizures evolving to generalized (grand mal) seizures
   - Simple partial (focal) seizures evolving to complex partial psychomotor seizures evolving to generalized seizures

II. Generalized seizures (convulsive and nonconvulsive)
   - Absence seizures
   - Typical absences (petit mal attacks)
   - Atypical absences (atypical petit mal attacks)
   - Myoclonic seizures
   - Clonic seizures
   - Tonic seizures
   - Tonic-clonic seizures (grand mal seizures)
   - Atonic seizures (clonic or atonic seizures)

III. Unclassified epileptic seizures

Defined by mode of onset

- Focal (partial) - begins in a part of one hemisphere
  - Simple partial (no impairment of awareness)
  - Complex partial (impairment of awareness / consciousness)

- Generalized, begins bilaterally
  - Convulsive vs. non-convulsive

- Unclassified: can be focal or generalized

- Focal seizures that subsequently evolve to generalized seizures are said to exhibit *secondary generalization*

Aura

- A remembered experience before loss of awareness: sinking, rising feeling in the stomach, palpitation, headache, limb movement, turning, remembering being somewhere, eye movement, hearing sounds, visual disturbance

*** Aura implies *focality* of seizure onset ***
Events masquerading as epileptic seizures

- Syncope & its related events
- Neurological disease (e.g. movement disorders, transient ischemic attacks, etc.)
- Behavioral disorders
- Sleep disorders
- Other …

_Pitfalls in the diagnosis and differential diagnosis of epilepsy_

--- Paediatrics and Child Health, 05/05/09

- High lights potential problems in differentiating various paroxysmal movement disorders
  (paroxysmal = sudden onset)
Pitfalls in the diagnosis and differential diagnosis of epilepsy
-- Paediatrics and Child Health, 05/05/09

• Epilepsy affects 1 in 200 children

• Appropriate management relies on accurate diagnosis

• Diagnosis is not based on any single diagnostic test

• Based on the history of attacks with support from investigation

Pitfalls in the diagnosis and differential diagnosis of epilepsy
-- Paediatrics and Child Health, 05/05/09

• The rate of misdiagnosis remains high; commonly due to the rush to make a diagnosis and lack of awareness of alternatives on the part of the assessor

• Assessment of children presenting with paroxysmal events should be undertaken by a pediatrician with expertise and training in epilepsy, working within a network linked to tertiary pediatric neurology
Common causes for recurrent seizures over the ages

<table>
<thead>
<tr>
<th>Age of onset</th>
<th>Probable cause</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Neonatal</td>
<td>Congenital malformation, birth injury, anoxia, metabolic</td>
<td>Adolescence (10-18 years)</td>
<td>Idiopathic epilepsy, trauma, drugs</td>
</tr>
<tr>
<td>Infancy (1-6 months)</td>
<td>As above, infantile spasms</td>
<td>Early adulthood (18-25 years)</td>
<td>Idiopathic epilepsy, trauma, neoplasm, drugs</td>
</tr>
<tr>
<td>Early childhood (6 months-3 years)</td>
<td>Infantile spasms, febrile sz, birth injury, infections, trauma, metabolic, toxin</td>
<td>Middle age (35-60 years)</td>
<td>Trauma, neoplasm, vascular disease, drugs</td>
</tr>
<tr>
<td>Childhood (3-10 years)</td>
<td>Birth injury, anoxia, infection, metabolic, idiopathic</td>
<td>Late life (over 60 years)</td>
<td>Vascular disease, neoplasm, abscess, degenerative dz, trauma</td>
</tr>
</tbody>
</table>

Febrile seizures

- Fever **without evidence** of intracranial infection or defined cause
  - 3 months to 5 years of age
  - 2%-5% in the United States
  - can run in the family

- Terminology:
  - simple febrile (<15 min, no focality)
  - complex febrile (prolonged, focality, or repetitive, associated with higher risk of non-febrile seizure disorder)
Generalized Tonic Clonic seizures

• Be aware that the description “GTC” seizure is an outward clinical manifestation
• “GTC” does not specify the mode of onset (focal vs generalized)

• Examples
  – Partial onset seizure with secondary generalization
  – Absence seizure, classified as Primary Generalized Epilepsy, which may or may not involve tonic clonic jerking movements

Not all GTC sz are the same, how to tell them apart

• History
  – particularly on presence of aura, any report of stereotypical movements with every seizure (e.g. hand movement, head or eyes deviation, dream like feeling, upset stomach, déjà vu feeling)

• EEG findings
Selected seizure syndromes

Generalized tonic clonic seizure
(aka “grand mal seizure”)

- Tonic phase (10-20 seconds):
  - Flexion of trunk, opening of mouth, eyelids, upward deviation of eyes, arms elevated, abducted, elbow semi-flexed, hand pronated
  - Followed by protracted extension phase of arms and legs, piercing cry, whole musculature is in spasm, breathing suspends, skin appears cyanotic, pupil dilated, bladder empties
GTC seizure

- Clonic phase

- Mild generalized tremor (which is repetitive relaxation of the tonic contraction)

- 8 per second, 4 per second, then violent flexor spasm, rhythmic, entire body, tongue biting

- Autonomic signs (e.g. pulse rapid, BP elevated, pupils dilated, salivation and sweating abundant, bladder pressure increases, remains apneic)

GTC seizure

- Terminal phase - all movements end

- Deep inspiration

- Deep coma

- Pupils may be equal or unequal; pupils begin to react to light

- Up to 5 minutes, then patient may open eyes, followed by confusion, or fall asleep exhausted
Simple partial seizure

- Focal onset
- Could have motor or sensory feature
- Consciousness preserved

Complex partial seizure

- Commonly arises from temporal lobe
- Awareness/consciousness impaired, dazed, or act inappropriately
- +/- collapse and/or convulsion
- Automatisms (e.g. lip smacking, fumbling of hands, shuffling of feet)
Absence Seizure

• “Petit mal”
• Brief, few motor activity
• Onset without warning
• Sudden interruption of consciousness
• Stares or briefly stops talking
• Patient sometimes not aware of them

Childhood Absence Epilepsy

• Peak age of onset: 4 - 8 years of age
  – range: 3-12 years

• Typical attacks last 5 to 10 seconds and occur up to 100 times each day

• No aura or post-ictal confusion
Absence Sz: other features

• Myoclonus, increased or decreased postural tone, picking at clothes, turning of the head

• ~50% of children with absence have at least one GTC seizure; may be 1st time brought to medical attention

• Hyperventilation almost always induces an absence seizure

• Over 90% remit by adolescence

Absence Seizures cont.

• Primary generalized

• EEG findings:
  – bilaterally synchronous & symmetrical
  – 3 Hz spike and slow waves
  – normal interictal background
Absence epilepsy

Unique focal motor/partial epilepsy of childhood

Convulsive disorder begins age 5-9, usually nocturnal, clonic contraction of face, one arm or leg

Self limited, disappears during adolescence
Juvenile Myoclonic epilepsy

- Primary generalized
- Onset about age 15, may persist into adulthood
- Brief muscle jerks, sometimes occur upon awakening

- May or may not lose consciousness, therefore patient sometimes not aware of seizure
- May be associated with absence seizure or other generalized seizure

Atonic seizure

- Primary generalized epilepsy
Infantile spasm

- Catastrophic seizure of childhood
- Severe EEG abnormality (hypsarrhythmia)
- Associated with mental impairment
- May be part of Lennox Gastaut syndrome, the most difficult of all forms of epilepsy to treat
- Triad of infantile spasm, EEG abnormality, mental retardation = West syndrome
- Sometimes seizure responds to ACTH

Mimickers of Seizures

- Syncope, convulsive syncope
- TIA
- Migraine
- Metabolic (e.g. hypoglycemia)
- Parasomnias (sleep disorders)
- Transient global amnesia
- Movement disorder
- Psychogenic spells
Pseudoseizures

- AKA non-epileptic seizure
- May co-exist in patient who has real seizures
- Associated with panic disorder, somatoform disorder, psychotic disorder, factitious disorder, malingering, victim of physical or sexual abuse
- Most do not consciously fake or produce these non-epileptic event
- Do not have EEG abnormality

Helpful clues:

- Purposeful behavior
- Side-to-side shaking of head
- Arms *not* moving during an apparent generalized seizure
- Reflex response to stimulus
- Erratic, non-stereotypical movement (true sz tends to be patterned and repetitive)
- Rapid recovery *without* confusion or fatigue
Seizure First Aid

- Protect airway, protect patient
- ABCs
- Do not put anything in patient’s mouth

Sz First Aid - specifics

- Keep calm and reassure other people who may be nearby.
- Don’t hold the person down or try to stop his movements.
- Time the seizure with a watch.
- Clear the area around the person of anything hard or sharp.
- Loosen ties or anything around the neck that may make breathing difficult.
- Put something flat and soft, like a folded jacket, under the head.
- Turn him or her gently onto one side. This will help keep the airway clear.
- Do not try to force the mouth open with any hard implement or with fingers. **A person having a seizure CANNOT swallow his tongue.** Efforts to hold the tongue down can injure teeth or jaw.
- Don’t attempt artificial respiration except in the unlikely event that a person does not start breathing again after the seizure has stopped.
- Stay with the person until the seizure ends naturally.
- Be friendly and reassuring as consciousness returns.
- Offer to call a taxi, friend or relative to help the person get home if he seems confused or unable to get home by himself.
Sz First Aid for children

- Stay calm & track time
- Keep child safe
- Do not restrain
- Do not put anything in mouth
- Stay with child until fully conscious
- Record seizure in log

**For tonic-clonic seizure:**
- Protect head
- Keep airway open/watch breathing
- Turn child on side

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Brief seizures

- An un-complicated generalized tonic clonic (grand mal) seizure in someone who has epilepsy is **not** a medical emergency, even though it looks like one
- It stops naturally after a few minutes without ill effects
- The average person is able to continue about his business after a rest period, and may need only limited assistance
When to call 911

- The seizure continues for more than five minutes.
- A second seizure starts shortly after the first has ended.
- Consciousness does not start to return after the shaking has stopped.
- Having breathing difficulties
- Seizure happened in water
- No medical I.D., no way of knowing whether the seizure is caused by epilepsy.
- The person is pregnant, injured, or diabetic.
- First-time seizure

Care in the ED

- ABCs
- Labs (e.g. CBC/Chem panel), anti-sz drug levels, tox screen, ABG
- Determine drug allergy status
- IV Glucose and thiamine
- Iv lorazepam, iv Dilantin
- Repeat above or versed, pentobarbital
Medical Evaluation

- Find out if sz is provoked (e.g. infection, alcohol withdrawal, sleep deprivation, drug use, trauma)
- Send labs (e.g. chem panel, blood glucose, ABG to r/o hypoxemia)
- Fever, Meningitis, encephalitis - LP
- Stroke
- Tumor
- Family history of seizure
- Brain hemorrhage, subarachnoid hemorrhage

Importance of physical examination

- May offer clue to cause of seizure
- Look at head and neck for size, shape, presence of scars, lumps or bumps, bruises, buits in the head, or dysmorphic features
- Don’t forget to check orthostatic blood pressure
- Skin may offer clue to a brain syndrome
  - Café au lait spot - Neurofibromatosis
  - Adenoma sebaceum – tuberous sclerosis
  - Nevus flammeus (port wine stain): Sturge-Weber syndrome
Essential elements of neurological examination

- Mental status
- Cranial nerves
- Motor
- Sensory
- Coordination
- Reflexes
- Gait

Mental Status

- Assess one’s awareness of surrounding
- Appropriateness of response
12 Cranial Nerves

- CN I, olfactory
- CN II, optic nerve
- CN III, IV, VI, oculomotor, trochlear, abducens
- CN V, trigeminal
- CN VII, facial
- CN VIII, auditory
- CN IX-X, glossopharygeal, vagus
- CN XI, accessory
- CN XII, hypoglossal

Sz eval continued:

- HEAD IMAGING
  - CT brain, ideally with contrast
  - If history suggests focal feature, then MRI

- EEG
  - If EEG abnormal (+ sz focus), then MRI

- Lumbar Puncture
  - Have low threshold for LP, esp fever or seizure with focal features; r/o Herpes encephalitis, other meningitis
Despite extensive investigation, up to 50% of seizures have no identifiable cause

Anti-epileptic Drugs (AEDs)

- Single seizure, generally don’t treatment unless:
  - Lesion identified on brain imaging
  - EEG shows focal epileptic discharge
    - (high probability of recurrence)
Selection of AEDs

- Most adult onset seizure has presumed focal onset, use traditional AED: Phenytoin, Carbamazepine, Phenobarbital

- Traditional AEDs don’t work in most Primary Generalized Epilepsy (e.g. absence seizures, myoclonic epilepsy)
- Instead use Broad spectrum AED (Lamotrigine, Valproic Acid, Topiramate, Levetiracetam)

- EEG helpful in determining seizure type and appropriateness of drug selection

Keep in mind

- Treat patient, not lab values
- Sometimes we may push the dose to supra-therapeutic range
- An abnormally high lab value does not always mean clinical toxicity, but it’s an important guide
Phone Triage for seizure

1. stable vs unstable patient
2. when, change in frequency?
3. duration
4. seizure type?
5. baseline seizure control (once a month/week/daily?)
6. Any recent med adjustment?
7. Any injury
8. current/recent illness or fever
9. current status (awake? breathing? playing?)
10. intervention/medical attention sought?

Vagus nerve stimulation (VNS)

• Involves repeated stimulation of the left vagus nerve through implanted electrodes
• First new mode of anti-epilepsy therapy
• Less than 10% seizure free

• Seizure Control
  – More than 75% in 34% pts
  – More than 50% in 60% pts
Types of Epilepsy surgery

• Lesionectomy - AV malformation, DNET, MTS

• Hemispherectomy
  – Sturge-Weber Syndrome
  – Rasmussen Syndrome

• Non-lesional resection
• Corpus Callosotomy

When to consider epilepsy surgery

• Refractory epilepsy

• Failed adequate trial of at least 3 antiepileptic drugs

• Lesion localizable – requires EEG telemetry
Special consideration for women of childbearing age

AED & contraception

- May reduce combined oral contraceptive (COC) efficacy (induce P-450 liver enzymes):
  - Phenobarbital
  - Phenytoin
  - Carbamazepine
  - Primidone
  - Topiramate
  - Oxcarbazepine

*Crawford, P; Interactions Between AED’s and Hormonal Contraception; CNS Drugs 2002; 16 (4): 263-272*
**Not Inducers of Liver Enzymes:**
consider COC use

- Valproic Acid
- Clonazepam
- Vigabatrin
- Lamotrigine
- Gabapentin
- Tiagabine
- Levetiracetam
- Zonisamide

**COC’s affect anticonvulsant levels**

- Valproic acid levels reduced by 50% with COC use in small case series; Lamotrigine reduce “significantly” as well
- Increased risk of seizure with VPA and COC use in single case report
- Largely uninvestigated

Some Say. . .

• Increase dose of estrogen in COC
• Usually 20-30 mcg ethinyl estradiol
• Plan over 50 mcg.
• Usual recommend barrier methods as well
• Over 80 mcg linked to 7-fold increased stroke risk from a low baseline risk in older studies

Bottom Line: AED’s and Hormonal Contraception

• Consider using: IUD, Condom, medroxyprogesterone acetate injections (DepoProvera®) every 10 weeks
Risks from a seizure during pregnancy

- Fetal heart rate slows during and for up to 20 minutes after a maternal convulsion, suggesting the presence of fetal asphyxia.

- The child of an epileptic mother convulsing during gestation is twice as likely to develop epilepsy as the child of a woman with epilepsy who does not convulse.

AED’s and Development

Developmental issues
- The neural tube closes 3-4 weeks
- Cleft lip exp before 5 wks
- Cleft Palate exp before 10 weeks
- Congenital heart disease before 6 weeks
Teratology

“Fetal Anticonvulsant” syndrome
  facial dimorphism
  cleft lip and palate
  cardiac defects
  digital hypoplasia
  nail dysplasia

Carbamazepine, phenytoin, primidone, and valproic acid
Trimethadione--contraindicated—fetal wastage

Holmes et al.; 2001--Prospective

Major Malformation of surgical, medical, or cosmetic importance
  • Normal, control population: 1.8%
  • One AED (Pht, Cbz, Pheno): 3.4-5.2%
  • Two or more AEDs 8.6%
  • Epileptic women NOT on AED 0%
  • Women taking AEDs with SZs 7.4-7.8%
Retrospective Studies

- Rate of major birth defects in the general population 2%-4.8%
- Infants of women with epilepsy to a rate of 3.5-6%
- Single AED increases the risk of congenital malformations to 4-8%
- 5.5% frequency of malformations with two anticonvulsant drugs, 11% with three anticonvulsant drugs, and 23% with the use of four AED's

Summary and conclusions as of 2008 from the registries

- Comparison of studies is DIFFICULT: different registries come to different conclusions in different populations for the same drugs
- Outcome data incomplete, lack of information from parents
- Risks of fetal malformations with newer AED’s is largely UNKNOWN and risks could be severe and lifelong

Risk of seizure during pregnancy

For the woman remaining seizure-free 9 months before pregnancy, there is an 84-92% chance of remaining free of seizures during pregnancy.


Despite incomplete data, current recommendations

• Avoid valproic acid in fertile women—multiple registries support incidence of major malformations (6.2%) higher than acceptable and lower IQ performance in children exposed during pregnancy
• Lamotrigine and carbamazepine—higher risk for cleft palate/lip (3.2 and 2.2% respectively. No evidence for IQ impairment of exposed children)

UK Registry data
Common Management Strategy

- Women with epilepsy should not be discouraged from becoming pregnant as the likelihood of having a healthy baby is high.
- Lowest AED dose that controls seizures several months before planned pregnancy
- Use most effective AED to control seizures
- Monotherapy
- Avoid sleep deprivation

Management strategy continued

- Supplement with folate 0.4 - 5 mg daily begin as long as 3 months before pregnancy until 12 weeks gestation
- Consider discontinuing AEDs prior to pregnancy for women whose seizures would not be expected to place her or her fetus at high risk.
- Avoid sudden cessation or lowering of AEDs by patient without physician consultation—maintain communication.
Vitamin K

- Previous recommendation: For patients taking phenytoin, phenobarbital, primidone, or ethosuximide or carbamazepine: Vitamin K 10-20 mg daily 2-4 weeks before delivery. Now shown to be of no known benefit
- Vitamin K 1 mg IM to infant on delivery to help reduce risk of neonatal intracerebral hemorrhage as in all infants

AED and breast milk

- Anticonvulsants are secreted in breast milk and ingested by the infant.
- Sedation and hyperirritability are reported.
- Withdrawal reactions from phenobarbital after lactational exposure
- Known health benefits of breast milk probably outweigh potential subtle and theoretical effects of AEDs
- Little information is available on newer anticonvulsants concerning their secretion into breast milk
- Use of these drugs while nursing must be individualized, considered in the context of known individual benefits over alternatives.
Strategies to reduce seizures and improve quality of life:

SAFETY TIPS AND TOOLS AND DAILY LIFE

Reduce Seizures

• Sleep Hygiene – enough sleep, regular sleep
• TLCs – therapeutic lifestyle choices
• Using medications correctly
• Avoid undue stress, infections, fevers, change in medication from name brand to generic (AAN position statement)
• Optimize other health conditions
Quality of Life

• IF you are going to live, LIVE
• Make every moment count
• The TLCs – therapeutic lifestyle choices
• Minimize changes in life due to seizures
• Avoid being labeled or labeling yourself as disabled.

Safety

• Identification: Medical Alert, info by Drivers License
• Activity limitations
• H1N1 vaccination
• Shower versus bath
• Wear seatbelt, wear bicycle helmet
• Know how to use rescue med like Diastat
• Keep extra medication with you and in earthquake kit
• Know what to do in a convulsion occurs
• Helmet for some
Driving

• All 50 states have laws requiring patients with epilepsy to be free of seizures for single fixed periods, with a median restriction of six months (range, 3 to 12 months).

• Some are more flexible, such as varying seizure-free restrictions based on individual clinical factors.

• California uses Medical Probation type II, type III, which specifies variable restriction of 3, 3-5, or >6 months of seizure control

• Source: Neurology 2001 57:1780, Epilepsy Foundation, DMV.CA.gov