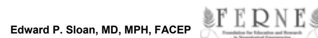
Optimizing Seizure and SE Patient Management in the Emergency Department

Edward P. Sloan, MD, MPH, FACEP 

Edward Sloan, MD, MPH

Professor

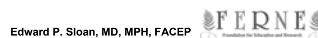
Department of Emergency Medicine
University of Illinois College of Medicine
Chicago, IL

Edward P. Sloan, MD, MPH, FACEP

Attending Physician
Emergency Medicine

University of Illinois Hospital
Our Lady of the Resurrection Hospital

Chicago, IL

Edward P. Sloan, MD, MPH, FACEP 

Global Objectives

- Improve pt outcome in seizures and SE
- Know how to quickly evaluate seizing pts
- Know clinically how to use protocols
- Provide rationale ED use of AEDs
- Facilitate useful disposition, documentation
- Improve Emergency Medicine practice

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Session Objectives

- Present a relevant patient case
- Consider seizure/SE protocols
- Review the ACEP 2004 guidelines
- Discuss the EFA recommendations
- Examine the SeizureStat© software
- Evaluate the patient outcome and ED documentation

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A Clinical Case

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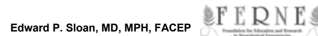

Patient Clinical History

- 37 yo male
- EMS to ED
- Generalized seizure at home,
- CFD: IV diazepam, resolved
- Hx TBI (remote) as seizure etiology
- On phenobarbiotal and dilantin
- Non-compliance in past
- No recent illness

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ED Presentation

- Post-ictal in ED
- Non-focal neurological exam
- No evidence of trauma or toxicity
- More appropriate, answers OK
- Has recurrent generalized seizure

- Is this patient an outlier?
- What is his optimal management?

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Why Do This Exercise?

- Status epilepticus is a medical emergency
- Few hospitals utilize a SE protocol
- A SE protocol improves patient outcome
- Guidelines exist that facilitate practice
- These efforts improve patient care, minimize risk, and enhance clinical practice

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Key Clinical Questions

- How do we define seizures and SE?
- What protocols exist that guide SE Rx?
- Are these protocols comparable?
- What do the ACEP guidelines tell us?
- What do the EFA recommendations state?
- How can SeizureStat© be used clinically?
- How can ED patient Rx be optimized?

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ED Seizure/SE Epidemiology and Classification

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Seizure Epidemiology

- Epilepsy in 1/150 people
- For each epilepsy pt, 1 ED visit every 4 years
- 1-2% of all ED visits
- Toxic/metabolic, febrile, non-compliance, trauma

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Seizure Mechanism

- Sz = abnormal neuronal discharge with recruitment of otherwise normal neurons
- Loss of GABA inhibition

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Status Epilepticus

- Seizure > 5- 10 minutes
- Two seizures without a lucid interval
- Assumes ongoing seizure activity during time of diminished responsiveness

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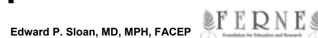

SE Pathophysiology

- Early compensation meets increased CNS metabolic needs (SBP, CBF ↑↑)
- Failure at 40-60 minutes, (SBP, CBF ↓↓)
- CNS tissue necrosis, adverse sequelae

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SE Pathophysiology

- Glutamate toxic mediator
- CNS necrosis even if systemic complications fully mitigated
- HTN, fever, rhabdomyolysis, hypercarbia, hypoxia, infection

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AMS in Seizures/SE

- Mental status should improve by 20-40 minutes
- If pt remains comatose, consider subtle SE & EEG
- Up to 20% of comatose pts in are in subtle SE

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Seizure Classification

- Generalized: both cerebral hemispheres
- Partial: one cerebral hemisphere (localized)

Generalized Seizures

- Convulsive: tonic-clonic
- Non-convulsive: absence

Generalized Seizures

- Primary generalized:
  starts as tonic-clonic seizure
- Secondarily generalized:
  tonic-clonic sz from a non-convulsive partial sz, ie aura (common)

Partial Seizures

- Simple partial:
  no impaired consciousness
- Complex partial:
  impaired consciousness

Specific Seizure Types

- Absence:
  petit mal
- Partial:
  Jacksonian, focal motor
- Complex partial:
  temporal lobe, psychomotor

SE Classification

- GCSE:

Generalized convulsive SE
Tonic-clonic motor activity

- Non-GCSE

Two Non-GCSE Types

- Non-convulsive SE:
  - Absence SE
  - Complex-partial SE
- Subtle SE:
  - Late generalized convulsive SE
  - Coma, persistent ictal discharge
  - Very grave prognosis

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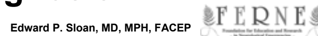

Subtle SE

- Severe insult, ie hypoxic
- Comatose
- Limited motor activity
- Mortality exceeds 50%
- Stop the seizure
- EEG confirmation

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Refractory SE

- No response to first-line drugs (Benzos, phenytoins)
- Severe CNS pathology
- 6-9% of all SE cases
- Overlap with subtle SE Dx??

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New-Onset Sz Recurrence

- 51% seizure recurrence risk
- 75% of recurrent seizures occur within 2 years of first sz
- Within 24 hours of ED visit: a small % will seize (1%)
- Partial, CNS abnormality: ↑↑ risk

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Seizure/SE Treatment Protocols

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SE Protocols

- Few published protocols
- Fewer studied protocols
- Limited evidence for single approach
- No other supporting data for one way

- Internet protocols exist
- Similar AEDs utilized
- Protocols provide guidance

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VA Coop Study

- Treiman, NEJM 1998
- Four treatments, 20 min endpoint
- GCSE, non-convulsive SE terminated

- Lorazepam 65%, phenobarbital 58%
- Diazepam and phenytoin 56%
- Phenytoin alone inferior 44%
- No use of fosphenytoin

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SE Review Article

- Lowenstein, NEJM 1998
- Timed AED therapy
- Lorazepam, a phenytoin, phenobarbital
- Midazolam or propofol infusion

- IV valproate not included in protocol
- Pentobarbital not an ED drug
- EMS: IM midazolam

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Pediatric SE Protocol

- Status Epilepticus Working Party
- British protocol, *Arch Dis Child*, 2000
- Lorazepam, a phenytoin, paraldehyde
- General anesthesia

- Phenobarbital, IV valproate not included
- No clear relationship to US practice
- Adult SE protocol applies in US

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ACEP Seizure/SE Clinical Policy

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Evidence Based Guidelines

- Define the clinical question
  - Focused questions best
  - Outcome measure must be determined
- Grade the strength of evidence
- Incorporate practice patterns, available expertise, resources and risk/benefit

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ACEP Clinical Policies

- Identify questions of clinical importance to ED practitioners
- Analyze the quality of data available related to disease state
- Differentiate anecdotal experience from practice supported by evidence

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ACEP Process

- Medical literature search
- Secondary search of references
- Articles graded
- Recommendations based on strength of evidence
- Multi-specialty and peer review

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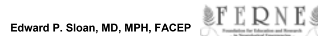

Evidence Strength

- Strength (Class) of evidence
  - I: Randomized, double blind interventional studies for therapeutic effectiveness; prospective cohort for diagnostic testing or prognosis
  - II: Retrospective cohorts, case control studies, cross-sectional studies
  - III: Observational reports; consensus reports
- Evidence strength downgraded if flawed methodologically

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Recommendation Strength

- Strength of recommendations:
  - A (Standard): High degree of certainty based on Class I studies
  - B (Guideline): Moderate clinical certainty based on Class II studies
  - C (Option): Inconclusive certainty based on Class III evidence, consensus

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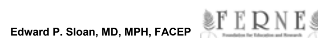

Seizure Clinical Policy

- Seizure patients frequently seen in the ED
- Sx of potentially life threatening diseases
- Potential morbidity and mortality
- ACEP Seizure Clinical Policy
  - 1993: Approach based
  - 1997: Revision
  - 2003: Critical questions; evidence based
  - 2004: Publication, *Ann Emer Med*, May

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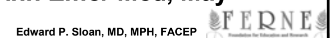

New Onset Sz: Lab Testing

What lab tests are indicated in the otherwise healthy adult patient with a new onset seizure who has returned to a baseline normal neurological status?

(outcome measure: abnormal lab that changes management)

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New Onset Sz: Lab Testing

- Level B recommendations:
  - Determine a serum glucose and sodium on patients with a first time seizure with no co-morbidities who have returned to their baseline
  - Obtain a pregnancy test in women of child bearing age
  - Perform a LP after a head CT either in the ED or after admission on patients who are immuno-compromised

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New Onset Sz: Neuroimaging

Which new onset seizure patients who have returned to a normal baseline require neuroimaging in the ED?

(outcome measure: abnormal CT)

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New Onset Sz: Neuroimaging

- Level B recommendations:
  - When feasible, perform a head CT of the brain in the ED on patients with a first time seizure
  - Deferred outpatient neuroimaging may be utilized when reliable follow-up is available

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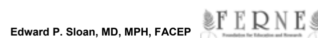
New Onset Sz: Dispo/AED Use

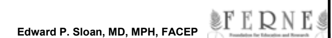
Which new onset seizure patients who have returned to normal baseline need to be admitted to the hospital and / or started on an AED?

(outcome measure: short term morbidity or mortality)

Edward P. Sloan, MD, MPH, FACEP 

New Onset Sz: Dispo/AED Use

- Level C recommendations:
  - Patients with a normal neurological examination can be discharged from the ED with outpatient follow-up
  - Patients with a normal neurological examination and no co-morbidities and no know structural brain disease do not need to be started on an anti-epileptic drug in the ED

Edward P. Sloan, MD, MPH, FACEP 

Sz/SE: Phenytoin Loading

What are effective phenytoin dosing strategies for preventing seizure recurrence in patients who present to the ED with a sub-therapeutic serum phenytoin level?

(outcome measure: short term seizure recurrence)

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Sz/SE: Phenytoin Loading

- Level C recommendation:
  - Administer an intravenous or oral loading dose of phenytoin or intravenous or intramuscular fosphenytoin, and restart daily oral maintenance dosing.

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Sz/SE SE Therapeutics

What agent(s) should be administered to a patient in status who continues to seize despite a loading dose of a benzodiazepine and a phenytoin?

(outcome measure: cessation of motor activity)

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Sz/SE SE Therapeutics

- Level C recommendation:
  - Administer one of the following agents intravenously: "high-dose phenytoin," phenobarbital, valproic acid, midazolam infusion, pentobarbital infusion, or propofol infusion.

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Sz/SE: EEG Monitoring

When should an EEG be performed in the ED?

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Sz/SE: EEG Monitoring

- Level C recommendation:
  - Consider an emergent EEG for patients suspected of being in non-convulsive SE or in subtle convulsive SE, for patients who have received a long-acting paralytic, or for patients who are in a drug-induced coma.

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ACEP Summary

- Evidence based clinical policies are useful tools in clinical decision making
- Policy does not create a "standard of care"
- Provides a foundation for clinical practice at a national level
- The current literature does not support the creation of any "level A" recommendations
  - 2 of the 6 clinical questions have sufficient evidence to support "level B" recommendations
  - 4 of the 6 recommendations are "level C"

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Epilepsy Foundation of American (EFA) Recommendations

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EFA Background

- Epilepsy Foundation of America
- Working Group on Status Epilepticus
- 1993 JAMA publication

- New literature will augment guidelines
- Evidence-based medicine mainstream
- American Academy of Neurology
- ACEP representatives part of process

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EFA Methods

- "…working group of experts…"
- "…develop a Rx protocol…"
- "…best medical Rx of convulsive SE."

- New medical info, evidence-based
- Revision will enhance consensus

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EFA Review, Consensus

- "Scientific evidence…given priority…"
- "…90 expert reviewers…"
- "…83 EFA chapter advisory boards…"

- Systematic grading of medical evidence
- Multiple societies now represented
- Better guidelines, broader consensus

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SE Rx Effectiveness

- "Over half of SE pts will respond…"
- "…remaining present an emergency…"
- "It is difficult to predict at presentation…"

- Majority of ED SE patients can be treated
- We cannot predict which will not respond
- Supports early, aggressive ED Rx

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SE Treatment Goals

- "…rapid termination of clinical and electrical seizure activity."
- "…longer SE…more difficult to control…"
- "…permanent…damage…duration SE."

- Refractory SE cases can't be predicted
- Aggressively terminate all seizures

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SE Treatment Approach

- "A clear plan
- Prompt administration
- Effective drugs
- Adequate doses
- Attention to hypoventilation"

- Every ED is able to effectively Rx SE

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EFA SE Conclusions

- Prolonged seizure duration
- Significant morbidity and mortality
- Multiple etiologies
- Varied outcome based on etiology
- Several Rx options are available
- More Rx today: fospht, IV valproate

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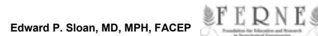

EFA SE Recommendations

- Provide timely, appropriate medical Rx
- Diagnose and treat simultaneously
- Stop the seizure
- Minimize adverse physiologic effects
- Have a predetermined plan
- Adhere to it

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SeizureStat©

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Key Learning Points: SeizureStat©

- FERNE software
- Provides various data
  - Written seizure/SE information
  - Therapies for urgent ED use
  - ACEP clinical policy recommendations
- Free from www.ferne.org website

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SeizureStat©

- Written seizure/SE information
  - 9 Seizure/SE topic areas
- Therapies for urgent ED use
  - 10 Therapies highlighted
- ACEP clinical policy recommendations
- Stat SE Treatment Protocol: 0-120 min

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Building SeizureStat©

- Satellite Forms
- MobileApps Designer
- Version 5.2.1
- Effective, laborious
- Need a roadmap
- Need clinical info

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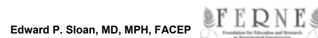
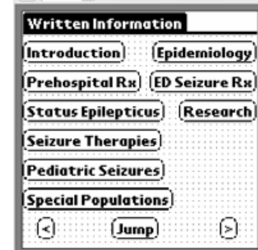
SeizureStat© Home Page

- Two intended uses
- Written info/learning
  - Text info
  - ACEP Clinical Policy
- Therapy info/Rx
  - Urgent Rx meds info
  - SE Protocol
  - Calculator



Written Information

- 9 Topics addressed
- Supports specific dosing data
- Assists in clinical decision-making

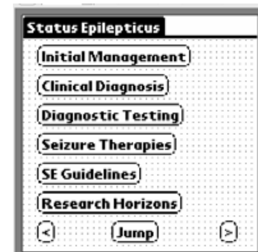


Seizure Therapies

- 6 Sections
- 5 Main therapies
- Written info
- Supports specific dosing data
- Accessed from Urgent Sz Meds pages

Status Epilepticus

- SE overview
- Written info
- Supports the SE Rx Protocol



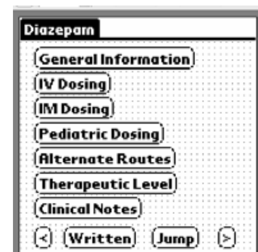
Urgent Seizure Meds Page

- 10 Therapies
- 6 Pages for each
  - General info
  - IV, IM doses
  - Therapeutic level
  - Alternate Routes
  - Clinical notes

Urgent Meds: Access Page

- Access thru 1st page
- Leads to 7 pages
- Specific med info
- Access to written info

- What's the dose?
- What to know?



Urgent Meds: General Info

- Trade names
- Pregnancy class
- Mechanism
- Pharmacokinetics
  - Onset of action
  - Duration of action

Diazepam - Information

Tradenames:
1) Diastat (gel)
2) Dizac (emulsion)
3) Valium (fluid)

Pregnancy Category: D

Mechanism: GABA Inhibution

Pharmacokinetics:
Onset of action: Minutes
Effect duration: 15 - 30 minutes

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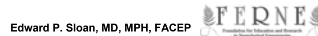

Urgent Meds: IV Dosing

- Single and total dose
- Unit doses
- Clinical notes

Diazepam - IV Dosing

Single dose 0.1 mg / kg
Total dose ~ 0.5 mg / kg

Unit dose 5-10 mg every 5 minutes
Total dose ~ 30 mg maximum

Clinical Notes:
* May repeat every 2-4 hours
* Do not exceed 5 mg / min
* Avoid small vein and extravesation

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Urgent Meds: IM Dosing

- Adult, pediatric doses
- Clinical notes

Diazepam - IM Dosing

Adult dose 0.1 mg / kg
Peditric dose:
Up to age 5: 0.2-0.5 mg / kg
Age 5 & older: 0.2 mg / kg

Clinical Notes:
* Peak concentration in one hour
* Inject deep into muscle
* Some IM bioavailabilty issues exist
* IM diazepam is not the preferred IM benzodiazepine in Seizure / SE

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Urgent Meds: Pediatric Dosing

- IV, IM doses
- Rectal dose
- Age-specific doses

Diazepam - Pediatric Dosing

IV
Up to age 5: 0.2 - 0.5 mg / kg
Age 5 & older: 0.2 mg / kg

IM
Up to age 5: 0.2 - 0.5 mg / kg
Age 5 & older: 0.2 mg / kg

Rectal
All ages 0.5 mg / kg

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Urgent Meds: Alternate Routes

- Rectal dose
- Endotracheal use
- Other routes
  - Sublingual
  - Intranasal
  - Buccal

Diazepam - Alternate Routes

Rectal
Adult dose: 0.2 mg / kg
Pediatric dose: 0.5 mg / kg

Endotracheal

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Urgent Med: Therapeutic Level

- Therapeutic level
- How does level change with dosing?
- Can level be exceeded? When?
- Clinical notes

Diazepam - Therapeutic Level

No clinically useful therapeutic levels are available

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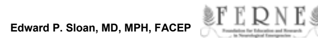
Urgent Meds: Clinical Notes

- The oral tradition in writing
- What are the relevant issues?
- How can the Sz med best be used?
- What problems can be encountered?
- How are problems treated?

Edward P. Sloan, MD, MPH, FACEP 

Stat SE Protocol: 0-90 Min

- Four 30 min periods
- 0-30 ABCs, Benzos
- 30-60 Phenytoins
- 60-90 Phenobarb, Valproate
- 90-120 Next page

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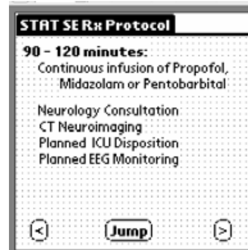
Stat SE Protocol: 90-120 Min

- 90-120 Continuous AED infusion
- Further Dx, Rx
- CT, neuro consult
- ICU Disposition
- EEG Monitoring



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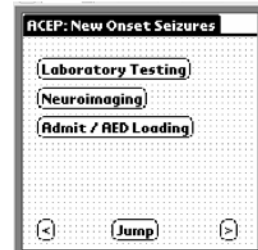
ACEP: New Onset Seizures

- 3 New onset sz topics
- Question stated
- Answer contains specific level A, B, C recommendations



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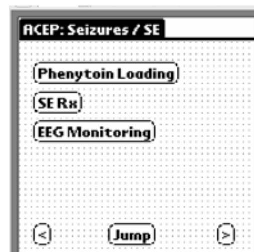
ACEP: Seizures/SE

- 3 Seizure/SE topics
- Question stated
- Answer contains specific level A, B, C recommendations



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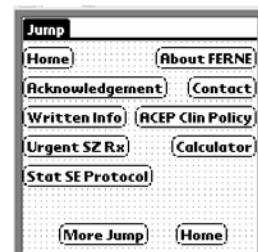
First Jump Page

- Access to relevant points within SeizureStat©
- Best way in which to navigate thru software



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Second Jump Page

- Access to more specific sites within SeizureStat©

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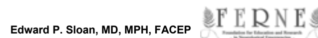

How to Use SeizureStat©

- Download from FERNE website
- Install on PDA
- Push many buttons
- Go frequently to the jump page
- Become familiar with protocol, meds
- In urgent need, get specific med data via *Home*, *Urgent Sz Meds* pages

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ED Treatment and Patient Outcome

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ED Patient Management

- Lorazepam 2 mg IVP x 6 over 25 min
- "I think the IV is out…"
- Generalized seizure continues
- IV access re-established
- Fosphenytoin 1 gram PE over 10 min
- Fosphenytoin 500 mg PE over 5 min
- Seizure ended, pt remained obtunded

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ED Diagnostic Evaluation

- Non-contrast CT negative
- Metabolic tests normal
- Toxicology screening negative
- Sub-therapeutic phenytoin level
- Sub-therapeutic phenobarbital level

- Diagnosis: Status Epilepticus

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Patient Outcome

- EEG in ICU, within 120 minutes
- Neuro consultation, no subtle SE
- Patient awoke completely in 12 hours
- Discharged from the ICU the next day
- No morbidity related to SE
- Discharged home two days later
- Told to take his meds as prescribed
- Neurology follow-up one week later

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Key Learning Points

- ED seizures, SE pts can be classified
- Seizure termination within 20-40 min critical
- Few published and proven protocols exist
- SE Rx: benzos, phenytoins, phenobarb
- Refractory SE: midazolam, propofol
- Similar approach applies to children

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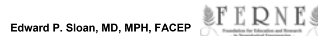

Key Learning Points

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Key Learning Points

- ACEP Clinical Policy:
  - Answers clinically important questions
  - New onset seizures, phenytoins, SE, EEG
- No level A recommendations
- EFA guidelines: no new SE protocol
- Have a protocol, utilize serial AEDs quickly
- Mg/Kg dosing, avoid unit dosing

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Key Learning Points

- SeizureStat© provides protocol, AED info
- Allows for rapid bedside Rx verification
- Provides timeline for optimal Rx
- FERNE: optimizing the care of ED patients
- www.ferne.org for free lecture downloads
- Neurological emergencies PDA software

Edward P. Sloan, MD, MPH, FACEP

Questions??

www.ferne.org
ferne@ferne.org

Edward Sloan, MD, MPH
edsloan@uic.edu
312 413 7490

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