Seizures, Epilepsy, Status Epilepticus, and Awake Craniotomy

A seizure is a common manifestation of many types of CNS diseases and is the external manifestation of epilepsy. A seizure results from an excessive discharge of large numbers of neurons that become depolarized in a synchronous fashion. Awake craniotomies are performed when tumors or epileptic foci lie close to cortical areas required for either speech or motor function or to mesiotemporal structures critical to short-term memory.

ANESTHETIC CONSIDERATIONS FOR EPILEPSY:

1. Pharmacokinetic and pharmacodynamic drug interactions in patients being treated with antiepileptic drugs.
2. Airway protection (risk of obstruction and aspiration if seizing)
3. Etiology (primary vs. secondary; congenital vs. acquired) and associated syndromes/ comorbidities
4. Medication management and optimization
5. Potential for perioperative seizures

ANESTTHETIC CONSIDERATIONS FOR AWAKE CRANIOTOMY:

1. Adequate analgesia and anesthesia during craniotomy conflicting with awake, comfortable and cooperative during cortical mapping.
2. Shared head space and potentially difficult airway access conflicting with high risk of apnea, airway obstruction, or inability to tolerate craniotomy.
3. Considerations of neurosurgery:
    a. Brain protection and relaxation
    b. Tight hemodynamic control to maintain CPP and precent increased ICP
    c. Rapid, smooth emergence to pre-anesthetic state
    d. Patient position and potential venous air embolism

ANESTHETIC GOALS FOR EPILEPSY:

1. Seizure termination if onset of pre-operative or intra-operative seizure.
2. Adequate ventilation, oxygenation, and maintenance of blood pressure.
3. Consider impact of antiepileptic drugs on organ function.
4. Consider effects of anesthetic drugs on seizures.

ANESTHETIC GOALS FOR AWAKE CRANIOTOMY:

1. Keep the patient comfortable during stimulating stages and awake/cooperative during mapping/resection.
2. Maintain oxygenation, ventilation, and cerebral perfusion pressure:
    - Prevent central apnea or hypopnea
    - Prevent obstructive airway
2. To select anesthetic techniques that produce minimal inhibition of spontaneous seizure activity.

HISTORY

- Age of diagnosis, how long they have had seizures/epilepsy
- The type and frequency of seizures (e.g., grand mal or absence)
- Specifics of symptoms such as staring or focal findings, prodrome
- Cause of seizures?
    - Brain tumors, aneurysms, arteriovenous malformations (AVMs), classic epilepsy, drug toxicity, electrolyte disorders, infections, and vascular disease from arteriosclerosis, stroke, sickle cell disease, or SLE
    - Adult-onset seizure is tumour until proven otherwise
- Evaluation and documentation of anticonvulsants and the adequacy of seizure control
- Side effects from antiepileptic medications (see Table 25-6 on next page)
    - All antiepileptic drugs can cause depression of cerebral function with symptoms of sedation
    - Long-term use of valproate is associated with increased surgical bleeding, especially in children (thrombocytopenia as well as valproate-induced decreases in von Willebrand factor and factor VIII)
    - Adverse hematologic reactions associated with antiepileptic drugs range from mild anemia to aplastic anemia and are most commonly associated with the use of carbamazepine, phenytoin, and valproate

PHYSICAL

- Focused neurological exam, document any deficits
- Level of consciousness and GCS
- Airway exam (for ease of intubation and ventilation – if difficult, may not want to do the case with sedation or without a protected airway)
- Signs of aspiration pneumonia
- Hypotension, cardiac arrhythmias (phenytoin)

INVESTIGATIONS

- CBCD, lytes, urea, Cr, glucose, tox screen, LFT's
    - Medications to control seizures have multiple side effects (bone marrow suppression, macrocytic anemia, leukopenia, hyponatremia), and testing should be directed at suspected abnormalities
- Anticonvulsant trough levels
    - Routinely ordering tests for serum drug levels of anticonvulsant medications is not indicated unless toxicity is a concern or the patient is having breakthrough seizures
- ABG if indicated
    - Topiramate inhibits carbonic anhydrase and can cause metabolic acidosis
    - Metabolic acidosis with ongoing seizures
- ECG/CXR if indicated

- EEG
    - Twenty-five percent of patients with a seizure have a normal electroencephalogram (EEG) when interictal
    - Thus, a negative EEG does not indicate that someone with a seizure will not have a withdrawal seizure when emerging from anesthesia
- MRI head is the preferred method for studying brain structure in patients with epilepsy (required for Stealth/neuronavigation)
- Standard electroencephalography is used to identify the location or locations of seizure foci as well as characterize their electrical properties
- Electrocorticography, where electrodes are surgically placed directly on the cerebral cortex, not only permits more accurate focus identification but also allows for mapping electrical events in the context of identifiable brain surface anatomy (a feature that will be valuable during surgical resection). Further, stimulation of various electrocorticographic electrodes will help identify eloquent brain areas prior to seizure focus resection, such that those areas can be avoided during surgery.
- The use of videography in addition to electroencephalography allows for the simultaneous documentation of electrical and clinical seizure activity
- Wada test: to localize the speech center (involves selectively anesthetizing the cerebral hemispheres, usually by injection of sodium amytal into the carotid artery to localize the hemisphere that controls speech or to confirm that there is bilateral representation for short-term memory, or both)

SURGICAL TREATMENT - SEIZURE FOCUS LOCALIZATION SURGERY

- Surgical treatment of seizure disorders is a consideration in patients who do not respond to antiepileptic drugs, or have unacceptable side-effects from combination drug therapy and/or inadequate seizure control
- Surgery is now being performed much earlier than in the past, particularly in young patients, to avoid social retardation resulting from medication side effects and persistent seizures
- Partial seizures may respond to resection of a pathologic region within the brain e.g., to remove a tumor, hamartoma, or scar tissue
- Corpus callosotomy may help to prevent the generalization of partial seizures to the alternate hemisphere
- Hemispherectomy is sometimes needed for persistent catastrophic seizures
- The most common operation is temporal lobectomy (permanent hemiparesis is a potential adverse effect of this surgery)
- A more conservative surgical approach to medically intractable seizures involves the implantation of a left vagal nerve stimulator (mechanism of effect unknown)

OPTIMIZATION

- Poorly controlled or new-onset seizures require consultation with a neurologist before proceeding with anything other than emergency surgery
- Patients receiving antiseizure medications should be maintained on their normal medication regimen until the time of surgery and administration resumed as soon as possible after surgery
- If intraoperative electrocorticography to identify seizure foci is intended, it is common to discontinue or reduce by half the anticonvulsants according to the perceived risk of uncontrolled seizures
- Aspiration prophylaxis
- For awake craniotomy, the patient should be educated about the nature and duration of the procedure and the limitations on patient movement

Table 25-6 Anticonvulsant Drugs

DRUG	SEIZURE TYPE	THERAPEUTIC BLOOD LEVELS (μg/mL)	SIDE EFFECTS*
Phenobarbital	Generalized	15–35	Sedation, increased drug metabolism
Valproate	Generalized Absence	50–100	Pancreatitis, hepatic dysfunction
Felbamate	Generalized Partial	20–140	Insomnia, ataxia, nausea
Phenytoin	Generalized Partial	10–20	Gingival hyperplasia Dermatitis Resistance to NM blockers
Fosphenytoin	Generalized Partial		Paresthesias Hypotension
Carbamazepine	Generalized Partial	6–12	Cardiotoxic, hepatitis Resistance to NM blockers
Lamotrigine	Generalized Partial	2–16	Rash Stevens-Johnson syndrome
Topiramate	Generalized Partial	4–10	Severe metabolic acidosis Hyperthermia
Gabapentin	Generalized Partial	4–16	Fatigue, somnolence
Primidone	Generalized Partial	6–12	Nausea, ataxia
Clonazepam	Absence	0.01–0.07	Ataxia
Ethosuximide	Absence	40–100	Leukopenia, Erythema multiforme
Levetiracetam	Generalized Partial	5–45	Dizziness, headache Somnolence
Oxcarbazepine	Partial	10–35	Hyponatremia, diplopia Somnolence
Tiagabine	Partial		Tremor, depression
Zonisamide	Generalized	10–40	Anorexia Decreased cognition

Partial listing NM, neuromuscular.

ANESTHETIC OPTIONS

- An epileptic patient requires no special anesthetic management other than that for the underlying disease, so for non-neurological surgeries, it can be done under Local/Regional/GA
- For seizure focus localization surgery, the anesthetic options are:
    - Awake for the entire surgery (Local)
        - The uncomfortable phases of the procedure are pin head holder placement (not all groups use a pin head holder), the craniotomy, and manipulation of the dura (in particular traction on subtemporal dura)
        - The actual manipulation of supratentorial brain parenchyma is painless
        - The volume of local anesthetic used to infiltrate pin sites and perform the scalp nerve blocks can be substantial (Keep in mind CNS toxicity with large doses of LA injection)
    - Asleep-awake-asleep
        - Performed when tumors or epileptic foci lie close to cortical areas required for either speech or motor function or to mesiotemporal structures critical to short-term memory
        - This anesthetic plan involves general anesthesia for the skin incision, initial craniotomy, and then for the closure in the end, while the patient is allowed to emerge from anesthesia for the middle portion of the surgery in which the surgeon is working around important structures
        - Need to have a cooperative and motivated patient
    - GA for the entire surgery

ANESTHETIC SETUP

- MONITORS:
    - Standard CAS monitors
    - Arterial line (if indicated)
    - Nerve stimulator
    - Temperature probe (hyperthermia with increased brain and muscle metabolism)
    - EEG and ECoG(for seizure focus excision)
- DRUGS:

- Standard emergency drugs
- Anti-epileptic drugs

- EQUIPMENT:
  - Airway equipment

MANAGEMENT OF ANESTHESIA

DRUGS:

- Management of anesthesia in patients with seizure disorders includes considering the impact of antiepileptic drugs on organ function and the effect of anesthetic drugs on seizures
- Except for gabapentin, all the useful antiepileptic drugs are metabolized in the liver before undergoing renal excretion (Gabapentin appears to have no in vivo metabolism and is excreted unchanged by the kidneys)
- Carbamazepine, phenytoin, and barbiturates cause cytochrome P450 enzyme induction,
  - Stimulation of the hepatic microsomal enzymes by anticonvulsants may increase the rate of biotransformation of volatile halogenated anesthetics and increase the risk of organ toxicity
  - Various antiepileptic drugs, specifically phenytoin and carbamazepine, via both pharmacokinetic and pharmacodynamic means, shorten the duration of action of nondepolarizing muscle relaxants
- Although most inhaled anesthetics, including nitrous oxide, have been reported to produce seizure activity, such activity during the administration of isoflurane and desflurane is extremely rare.
  - These drugs generally produce a dose-dependent depression of EEG activity
  - However, sevoflurane may be epileptogenic, although the clinical significance of this finding is uncertain
- Potent opioids such as fentanyl, sufentanil, alfentanil, and remifentanil may produce myoclonic activity or chest wall rigidity that can be confused with seizure activity
- Co-existing sedation produced by antiepileptic drugs may have additive effects with anesthetic drugs
- When selecting anesthetic induction and maintenance drugs, one must consider their effects on central nervous system electrical activity
  - Methohexital can activate epileptic foci and has been recommended as a method for delineating these foci during electrocorticography in patients undergoing surgical treatment of epilepsy
  - Ketamine may produce seizure activity in patients with known seizure disorders
  - Alfentanil, ketamine, enflurane, isoflurane, and sevoflurane can cause epileptiform spike-and-wave electroencephalographic activity in patients without a history of seizures, but are also known to suppress epileptiform and epileptic activity
  - Most inhaled anesthetics, including nitrous oxide, have been reported to produce seizure activity. The presence of halogen atoms is an important determinant of the convulsant properties of volatile anesthetics, with fluorine being incriminated as epileptogenic
  - Seizures and opisthotonos have rarely been observed following propofol anesthesia, suggesting caution when administering this drug to patients with known seizure disorders
  - When selecting muscle relaxants, the central nervous system–stimulating effects of laudanosine, a proconvulsant metabolite of atracurium and cisatracurium, may merit consideration
  - It seems reasonable to avoid administering potentially epileptogenic drugs to patients with epilepsy.
  - Instead, thiobarbiturates, opioids, and benzodiazepines are preferred. Isoflurane, desflurane, and sevoflurane seem to be acceptable choices in patients with seizure disorders

INDUCTION

- Premedicants with an anticonvulsant effect (e.g., benzodiazepines) should not be used because they may interfere with intraoperative EEG localization

MAINTENANCE

- The Asleep-Awake-Asleep anesthetic plan can be done in many ways
  - The asleep portions of the procedure may be performed without an airway, with a laryngeal mask airway (LMA), or with an endotracheal tube in place
    - An endotracheal tube provides the most secure airway, but it is also the most difficult to remove during the procedure, particularly with the patient's head secured in rigid fixation (topical lidocaine to the larynx and trachea prior to placement can minimize coughing as the patient emerges)
    - An LMA is a suitable alternative to no airway as it can frequently be removed with little movement of the patient as he or she emerges from anesthesia (topical application of lidocaine to the airway prior to insertion of the LMA supplemented with lidocaine jelly on the LMA may improve patient tolerance during emergence)
  - For suitable candidates, the asleep portions may be performed with spontaneous ventilation with propofol infusion
    - Straightforward emergence with minimal coughing, gagging, or straining, and decreases the incidence of nausea and vomiting during the awake period
    - Can also run a combination of propofol with fentanyl or remifentanil in low dose, but be careful of respiratory depression if the patient's head is in pin fixation which severely restricts ability for quick airway intervention
    - Propofol should be discontinued at least 15 minutes before EEG recording
    - Despite prompt awakening, propofol leaves a residual EEG "footprint" characterized by high-frequency, high-amplitude beta activity, which can obscure the abnormal activity that is being sought in the cortical surface EEG
  - During the awake portion of the procedure, cortical surface EEG recording is performed to locate the seizure focus
    - All sedatives are typically withheld, but for particularly stimulating events (e.g., drilling) and in coordination with the surgeon, small boluses of propofol or fentanyl may be given
    - Give antiemetics to prevent nausea
    - If no seizure activity is observed, provocative maneuvers may be requested:
      - Methohexital in a dose of approximately 0.3 mg/kg is generally safe and effective
      - Etomidate, approximately 0.05 to 0.1 mg/kg, also has been used
  - After localization by EEG, functional testing may be performed by stimulating the cortical surface electrically and observing for motor, sensory, or speech interruption effects
    - During stimulation, be prepared to treat grand mal convulsions when they are not self-limited (e.g., with propofol in 0.5 to 1 mg/kg increments)
    - Propofol should be withheld, however, until it is clear that the seizure is not going to terminate spontaneously because propofol may interfere with subsequent EEG localization of the seizure focus for some time.
  - Following this critical portion of the surgery, the patient may be fully anesthetized for the surgical closure
    - Initiating a propofol infusion and continuing with spontaneous ventilation is again a good option

        - Otherwise, manipulation of the airway to place an LMA or endotracheal tube will be necessary while avoiding the sterile field
- If GA is given for the entire surgery, localization of seizure focus also can be accomplished during light general anesthesia (e.g., N_2O/fentanyl/low-dose isoflurane)
    - During general anesthesia, alfentanil in a bolus dose of 30 to 50 mcg/kg, etomidate in doses of 0.2 to 0.3 mg/kg, and remifentanil in a bolus dose of 2.5 mcg/kg have been reported to be effective in activating seizure foci

EMERGENCE

- Quick emergence to allow assessment of neurological function
- Seizure symptoms such as staring and obtundation may be misinterpreted as residual anesthetic effects in the postoperative period

DISPOSITION & MONITORING

- Neurological assessment in OR or recovery
- Neurosurgery ICU post-op

COMPLICATIONS

- Requirement for emergency airway control due to:
    - Airway obstruction
    - Apnea
    - Uncooperative patient
    - Requirement for induction of GA due to unsatisfactory anesthesia reported in 2-16%
    - May pose a significant challenge given patient usually affixed in pins, and may be positioned lateral
    - Always have LMA available
- Nausea and vomiting
- Seizures
- Cardiac dysrhythmias (bradycardia common), can occur during stimulation of deep structures (hypothalamus)
- LA toxicity
- Patient movement and discomfort
- Other general neurosurgical problems: venous air embolism, intracerebral hemorrhage, neurological defect

PATHOPHYSIOLOGY

- A seizure is the term for the clinical event defined as a paroxysmal alteration in neurologic function caused by a synchronous, rhythmic depolarization of brain cortical neurons
- Epilepsy is defined as recurrent seizures resulting from congenital or acquired (e.g., cerebral scarring) factors; it affects approximately 0.6% of the population
- Seizure is one of the most common neurologic disorders and may occur at any age
- Six percent to 10% of individuals younger than 70 years will experience a seizure at some time during their lifetime
- Fifty percent to 70% of patients with one seizure will never have another
- 70% of people with two seizures will have an epileptic focus, be candidates for antiseizure medications, and be subject to withdrawal seizures after anesthesia if such medications are not continued
- Clinical manifestations depend on the location and number of neurons involved in the seizure discharge and its duration
- Seizures are currently classified based on two factors: loss of consciousness and focus of seizure activation
    - Simple seizures involve no loss of consciousness, whereas altered levels of consciousness are seen in complex seizures
    - Partial seizures appear to originate from a limited population of neurons in a single hemisphere, whereas generalized seizures appear to initially involve diffuse activation of neurons in both cerebral hemispheres
    - A partial seizure may be initially evident in one region of the body (i.e., the right arm) and may subsequently become generalized, involving both hemispheres, a process known as the jacksonian march
- The most frequently encountered types of seizures are:

1. *Grand mal seizure*: A grand mal seizure is characterized by generalized tonic-clonic activity. All respiratory activity is arrested and a period of arterial hypoxemia ensues. The tonic phase lasts for 20 to 40 seconds and is followed by the clonic phase. In the postictal period, the patient is lethargic and confused. Diazepam and thiopental are effective for treatment of acute, generalized seizures. Epileptic patients resistant to drug therapy may benefit from surgical resection of a seizure focus or vagal nerve stimulator implantation.
2. *Focal cortical seizure*: Focal cortical seizures may be sensory or motor, depending on the site of neuronal discharge. There is usually no loss of consciousness, although the seizure activity may spread to produce a grand mal seizure.
3. *Absence seizure (petit mal):* Absence seizures are characterized by a brief loss of awareness lasting 30 seconds. Additional manifestations include staring, blinking, and rolling of the eyes. Absence seizures typically occur in children and young adults.
4. *Akinetic seizure:* Akinetic seizures are characterized by a sudden, brief loss of consciousness and postural tone. These types of seizures usually occur in children and can result in severe head injury from a fall.
5. *Status epilepticus:* Status epilepticus is defined as two consecutive tonic-clonic seizures without regaining consciousness, or seizure activity that is unabated for 30 minutes or more. Grand mal status epilepticus typically lasts for 48 hours with a seizure frequency of four to five per hour; mortality can be as high as 20%. As the seizure progresses, skeletal muscle activity diminishes and seizure activity may be evident only on the electroencephalogram (EEG). Respiratory effects of status epilepticus include inhibition of the respiratory centers, uncoordinated skeletal muscle activity that impairs ventilation, and abnormal autonomic activity that produces bronchoconstriction. There is a high likelihood of permanent neuronal damage from continued seizures.

- During generalized seizure activity, CMR and CBF may increase dramatically
    - The intensive motor and brain activity associated with generalized seizures leads to the development of systemic and cerebral acidosis, often accompanied by a reduction in arterial oxygenation, an increase in $Paco_2$, and peripheral lactic acidosis
    - If generalized seizure activity continues unabated, arterial hypotension ensues
    - With muscular relaxation and measures ensuring adequate oxygenation and ventilation, the systemic acidosis and hypotension can be avoided and the severity of the cerebral acidosis diminished
    - During relatively brief episodes of continuous seizures, the brain seems able to meet the high metabolic demands. However, even with effective ventilation and maintenance of perfusion pressure, when seizures continue for a prolonged period, they can lead to the development of irreversible neuronal damage
    - Therapy aimed at interrupting the seizure and restoring a normal balance between cerebral metabolic demand and blood flow is indicated. Barbiturates, benzodiazepines, or other potent anticonvulsants are appropriate. Adequate ventilation, oxygenation, and maintenance of blood pressure are important adjunctive measures. Muscle relaxants must be viewed as purely symptomatic therapy because they do not alter the abnormal cerebral electrical activity.

- Epileptic seizures can arise from discontinuation of sedative-hypnotic drugs or alcohol, use of narcotics, uremia, traumatic injury, neoplasms, infection, congenital malformation, birth injury, drug use (e.g., amphetamines, cocaine), hypercalcemia or hypocalcemia, blood in the ventricle or hypoxia, and vascular disease and vascular accidents
- Transient abnormalities of brain function, such as occurs with hypoglycemia, hyponatremia, hyperthermia, and drug toxicity, typically result in a single seizure; treatment of the underlying disorder usually is curative

MANAGEMENT OF STATUS EPILEPTICUS PATIENT:

- Status epilepticus is a life-threatening condition that manifests as continuous seizure activity or two or more seizures occurring in sequence without recovery of consciousness between them
- The goal of treatment of status epilepticus is prompt establishment of venous access and subsequent pharmacologic suppression of seizure activity combined with support of the patient's airway, ventilation, and circulation
- Diagnose seizure and prevent traumatic injury to the patient
- Tracheal intubation may be needed to protect the patient's lungs from aspiration and to optimize delivery of oxygen and removal of carbon dioxide.
    - Long-acting muscle relaxants should be avoided if muscle movement, independent of electrophysiologic monitoring, is the principal endpoint for assessing therapy effectiveness.
    - Usually, administration of an antiepileptic anesthetic, such as propofol or thiopental, will temporarily halt seizure activity during tracheal intubation.
- If respiratory distress, apnea or loss of consciousness occurs:
    - Establish patent airway, position, consider intubation if necessary
    - Administer 100% O2 by nasal cannulae or mask, assist ventilation as necessary
    - Do not hyperventilate the patient as this would decrease the seizure threshold
- Initiate monitoring of vitals and EKG
- Monitoring arterial blood gases and pH may be useful for confirming the adequacy of oxygenation and ventilation.
- Ensure adequate IV access and draw bloodwork
    - If hypoglycemic or unable to assess: 1 amp of D50W iv (peds 2 mL/kg of D25W) followed by thiamine 100mg IM, administer MgSO4 to parturients with eclampsia
    - Hypoglycemia can be ruled out as a cause within minutes using rapid bedside glucose assessment techniques. If present, it can be corrected by intravenous administration of 50 mL of 50% glucose. Routine use of glucose infusion prior to confirming preexisting hypoglycemia is not recommended as hyperglycemia can exacerbate brain injury.
    - Correct electrolyte imbalance
- Administer first-line anticonvulsant benzodiazepine:
    - Midazolam 0.5 mg iv increments
    - Diazepam 0.2 mg/kg at 5 mg/min iv (peds 0.3 mg/kg iv, 0.6 mg/kg pr to max 20 mg)
    - Lorazepam 0.1 mg/kg at 2 mg/min iv (peds 0.05-0.1 mg/kg iv/pr, max 4 mg)
    - Avoid overdoses as they may cause respiratory or myocardial depression and may prolong the postictal state
- If intraoperative, administer propofol 30 mg iv or thiopental 1-4 mg/kg iv stops most intractable seizures
- Administer second-line anticonvulsants:
    - Phenytoin 20 mg/kg iv infusion at 50 mg/min (administer slowly to avoid cardiovascular depression)
        - Pediatric loading dose 15-20 mg/kg
        - Monitor bp and ECG
        - Incompatible with glucose containing solutions
    - Phenobarbital 5-10 mg/kg boluses (maximal dose 20 mg/kg)
        - Neonate 20-30 mg/kg iv, pediatric 15-20 mg/kg iv + additional 5-10 mg/kg if necessary
        - Causes respiratory depression and will most likely need ventilation
    - Paraldehyde 0.3 mL/kg can be given rectally
- If status epilepticus persists, need a neurology consult, a monitored bed in ICU and patient should be intubated with a short-acting neuromuscular blocker (convulsions used to monitor seizure activity)
    - Seizure should be treated with a general anesthetic: midazolam, propofol, thiopental, ketamine, etomidate, and if scavenging available, isolflurane
    - Patient will most likely require vasopressors
    - Initiate neuromuscular blockade if necessary: allows adequate ventilation and oxygenation, avoids or controls complications of excessive muscular activity, increased peripheral oxygen consumption, risk of injury in the presence of an unstable neck fracture, laceration of the tongue
- Metabolic acidosis is a common sequela of ongoing seizure activity. In such instances, intravenous sodium bicarbonate may be needed to treat extreme acid-base abnormalities.
- Hyperthermia associated with muscle hyperactivity and increased brain metabolism occurs frequently during status epilepticus and necessitates active cooling.

CONSIDERATIONS IN PREGNANCY

- ~0.5% of all parturients have chronic seizure disorder
    - One third experience increase in seizure frequency and half experience no change
- Increase in seizure frequency in pregnant women may be due to lowering seizure threshold: increased estrogen, increased Na and H2O retention, increased stress and anxiety
- Anticonvulsant drug levels decrease during pregnancy (despite increased dose)
    - Decreased protein binding and increased clearance
- Oral antiepileptic therapies should be continued whenever possible throughout the peripartum period
- For surgery, anticonvulsant medications should be given in the therapeutic range and continued through the morning of surgery in pregnant women; they should also be given postoperatively, even in mothers who plan to breast-feed, according to guidelines published by the American Academy of Neurology
- Hypoxia and acidosis during generalized seizure can result in fetal distress and intrauterine fetal death
    - Suggested epileptics have 2-fold increase in preeclampsia, preterm labour and placental abnormalities
- Infants of mothers with epilepsy are approximately twice as likely to have adverse pregnancy outcomes, including intrauterine fetal death, cesarean delivery, neonatal and perinatal death, low birth weight, and abnormal development
    - The risk of congenital malformations is approximately 4% to 6%
    - Malformations have been associated with all currently used therapeutic modalities; those most often seen are cleft lip and palate, and cardiac, neural tube, and urogenital defects
    - Certain drugs have been associated with a higher relative risk of congenital defects than others
    - Data from prospective studies indicate that phenobarbital and valproate are associated with significantly higher rates of major malformations

- Infants of mothers undergoing long-term antiepileptic therapy are at risk for a deficiency in vitamin K–dependent clotting factors
    - Antiepileptic agents that are enzyme inducing (e.g., phenytoin, phenobarbital, carbamazepine) are most likely to cause this problem. These drugs cross the placenta and may increase the rate of oxidative degradation of vitamin K in the fetus.
    - Affected infants are at risk for neonatal hemorrhage and respond to vitamin K (1 mg) given intramuscularly at birth
- If the patient experiences a seizure during labor, airway protection and support of ventilation are essential
    - Small doses of a benzodiazepine or sodium thiopental stop most seizures
    - Fetal bradycardia may necessitate immediate delivery
- Regional/neuraxial anesthesia is not contraindicated
- If GA, avoid ketamine, enflurane, and meperidine (may lower seizure threshold)
    - Induction of general anesthesia can be performed with sodium thiopental and succinylcholine, and anesthesia may be maintained with a mixture of oxygen, nitrous oxide, and isoflurane
    - Avoid hyperventilation (reduces cerebral blood flow without a reduction in cerebral metabolic rate) and avoid hypoventilation (associated with hypercarbia, which can lower the seizure threshold)
    - In order to prevent further neurologic injury, it is important not to be overly aggressive in the reduction of systemic pressure, because cerebral perfusion pressure equals mean arterial pressure minus intracranial pressure
    - Avoidance of hypoxia, hyperthermia, and hyperglycemia are also important in avoiding an exacerbation of neurologic injury
    - Patients who have not recovered neurologically should remain intubated and should be monitored in an intensive care unit; If unconsciousness persists, further neurologic evaluation, including EEG and CT should be performed.
    - Some physicians recommend the avoidance of meperidine for postoperative analgesia because of one report of myoclonic seizures in several patients who had received this agent
- Eclampsia:
    - Seizures have an abrupt onset, typically beginning as facial twitching that is followed by a tonic phase persisting for 15 to 20 seconds. This progresses to a generalized clonic phase characterized by apnea, which lasts approximately 1 minute. Breathing generally resumes with a long stertorous inspiration, and the patient enters a postictal state with a variable period of coma
    - Cardiorespiratory arrest and pulmonary aspiration of gastric contents can complicate a seizure
    - Although the definitive diagnosis for eclampsia is a sudden seizure in a pregnant woman who has signs and symptoms of preeclampsia, a woman who lapses into coma without witnessed convulsions can also be classified as eclamptic
    - The mechanism of eclamptic seizures remains poorly understood
        - One hypothesis involves a loss of the normal cerebral autoregulatory mechanism that results in hyperperfusion and leads to interstitial or vasogenic cerebral edema and decreased cerebral blood flow
        - Neuroradiologic studies suggest that eclampsia might be a form of reversible posterior leukoencephalopathy syndrome (PLES) or posterior reversible encephalopathy syndrome (PRES)
            - The difference between PLES and PRES is that significant blood pressure elevations are not necessarily present in PRES
    - Until proven otherwise, the occurrence of seizures during pregnancy should be considered eclampsia. Conditions that simulate eclampsia include seizure disorder, stroke, hypertensive encephalopathy, ischemia or hypoxia, cerebral space-occupying lesion, systemic disease (e.g., systemic lupus erythematosus, sickle cell anemia), infection (e.g., meningitis, encephalitis), electrolyte and endocrine disturbances, PRES or PLES, vasculitis or angiopathy, amniotic fluid embolism, medications (withdrawal, illicit drug use), and organ failure

CHESTNUT:

BOX 45-5

Eclampsia: The ABCs of Seizure Control

Airway

- Turn patient to left side; apply jaw thrust.
- Attempt bag and mask ventilation (F_{IO2} = 1.0).
- Insert soft nasopharyngeal airway if necessary.

Breathing

- Continue bag and mask ventilation (F_{IO2} = 1.0).
- Apply pulse oximeter and monitor Sa_{O2}.

Circulation

- Secure intravenous access.
- Check blood pressure at frequent intervals.
- Monitor electrocardiogram.

Drugs

- Magnesium sulfate:
    - 4 to 6 g IV over 20 minutes
    - 1 to 2 g/hr IV for maintenance therapy
    - 2 g IV, over 10 minutes, for recurrent seizures
- Antihypertensive agents:
    - Labetalol 10 to 20 mg IV or hydralazine 5 to 10 mg IV as needed to treat hypertension

TABLE 49-2 -- Classic Antiepileptic Drugs Used during Pregnancy

Drug	Dose	Therapeutic Serum Level	Side Effects	Toxicity	Types of Seizures*		
					Tonic-Clonic	Absence	Complex Partial
Phenytoin (Dilantin)	Average: 400 mg/day Range: 300-1200 mg/day	10-20 µg/mL	Ataxia Drowsiness Gum hyperplasia Hypertrichosis Nystagmus	Rash Serum sickness Pseudolymphoma Stevens-Johnson syndrome Lupus erythematosus Macrocytic anemia Rare hepatic or marrow toxicity Cerebellar degeneration Peripheral neuropathy	+	–	+
Phenobarbital	Average: 120 mg/day Range: 30-210 mg/day	10-35 µg/mL	Drowsiness Ataxia Nystagmus	Rash Possible teratogenicity	+	–	+
Primidone (Mysoline)	Average: 1000 mg/day Range: 500-2000 mg/day	4-12 µg/mL	Drowsiness Nausea Ataxia Nystagmus (Tachyphylaxis typical)	Rash Adenopathy Lupus erythematosus Macrocytic anemia Arthritis Edema	+	–	+
Carbamazepine (Tegretol)	Average: 600 mg/day Range: 200-1200 mg/day	4-8 µg/mL	Drowsiness Dizziness Blurred vision Ataxia Gastrointestinal disturbance	Blood dyscrasia (rare)	+	–	+
Ethosuximide (Zarontin)	Average: 1000 mg/day Range: 500-2000 mg/day	40-100 µg/mL	Nausea Abdominal pain Drowsiness Personality change Headache	Rash Nephropathy Bone marrow depression	–	+	–
Clonazepam	Average: 3 mg/day Range: 1.5-20 mg/day	0.01-0.07 µg/mL	Drowsiness Dizziness Ataxia	Coma	+	+	+

Modified from Dalessio DJ. Current concepts: Seizure disorders and pregnancy. N Engl J Med 1985; 312:559-63.

*A plus sign (+) denotes that the drug is useful in the indicated form of seizure; a minus sign (–) indicates that it is not.

REFERENCES

- Barash Chpt 25, 39
- Coexisting Chpt 10
- Miller Chpt 13, 34, 35, 36, 63
- Chestnut Chpt 45, 49