Appendix 1: Protocol for the Management of Seizures

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Definition

A seizure is a manifestation of an excessive discharge of hyper-excitable cerebrocortical neurons. The appearance of seizures varies with the location and extent of seizure activity. Seizures are generally classified according to their clinical manifestations.

Generalized seizures have widespread onset within both cerebral hemispheres, and manifest in the following manner

- Loss of consciousness
- Recumbency
- Generalized motor signs, including convulsions, tonic (sustained) or clonic (repetitive) muscle contractions, limb paddling, and trembling.
- Jaw chomping and facial twitching.
- Autonomic hyperactivity including pupillary dilatation, salivation, piloerection, micturition, and defecation.
- Occasionally, atonic seizures occur, which must be distinguished from syncope and narcolepsy-cataplexy

Partial seizures have a focal onset in one cerebral hemisphere, and limited spreading within the brain. Their occurrence indicates the presence of acquired structural deformity. Partial seizures may be either simple or complex, depending on whether consciousness is disturbed.

Simple partial seizures manifest in the following manner

- Unilateral motor signs such as facial twitching, tonic or clonic movements of one or both limbs on one side, spasmodic turning of the head to one side. Movements are contra-lateral to the side of the lesion or seizures focus.

Complex partial seizures spread to allocortical areas, and consciousness is either lost or impaired. Other symptoms of complex partial seizures include

- Contra-lateral or bilateral asymmetric or symmetric motor signs, usually limited to a particular area of the body; for example twitching, jaw chomping, tremor of the neck.
- Bizarre behaviors, growling, hissing, circling, panic, or attacking real or imaginary objects.
- Consciousness is diminished or lost, however, seizure motor activity is usually not sufficient to cause recumbency.
- Presence of aura. Aura corresponds to the onset of a simple partial seizure before it evolves into a complex partial seizure or generalized seizure.
- Localized post-ictal motor deficits may occur in partial seizures, and occurs on the contra-lateral side to the seizure focus.

Pathophysiology

- Seizures result from an imbalance between the normal excitatory and inhibitory mechanisms of nervous tissue in the brain. Idiopathic seizures result from a functional disturbance in the neurons. Primary intra-cranial causes of seizures usually result from lesions that irritate the surrounding neurons, for example neoplasia, glial scarring following trauma. Extracranial causes of seizures alter brain biochemical homeostasis in favor of excitation.
- Seizures cause increased cerebral metabolic rate, increasing the rate of oxidative metabolism. This causes elevated carbon dioxide production, potentiating CNS acidosis and resultant CNS edema due to local vasodilatation. Increased cerebral metabolism results in decreasing PO_2 and oxygen deficiency. Neuronal calcium concentrations increase, and arachadonic acid metabolites, prostaglandins, and leukotrines lead to brain edema and cell death. Elevated CSF pressure may also result
- Systemic signs – Sympathetic nervous system activation and adrenal release of catecholamines result in hyperglycemia, hypoglycemia, hyperthermia, dehydration, lactic acidosis, cardiac arrhythmias, pulmonary hypertension, edema, and hemorrhage.

Management

- **Airway**
  - Secure a patent airway
  - Provide oxygen by flow past system
  - Orotracheal intubation reduces the chances of aspiration of gastric and oral secretions and blood

- **Breathing**
  - Assess mucous membrane color
  - If patient comatose, intubate and provide supplemental oxygen
  - If patient is semi-comatose, anesthetize with thiobarbituate or propofol, intubate and ventilate; provide supplemental oxygen.
  - If patient is conscious, provide oxygen if ventilating adequately; if not, consider anesthetizing and ventilating

- **Patient Assessment**
  - Airway and breathing as above
  - Auscultate heart, determine heart rate, assess pulses
  - Determine patient temperature
  - Observe the seizure - symmetrical and generalized vs. focal and asymmetrical. Lateralizing signs (head tilt, turning to one side, unilateral twitching or clonus) are suggestive of secondary epilepsy.

- **Circulation and Data Collection**
  - Place cephalic catheter and begin fluid therapy with LRS to replace intravascular volume deficits.
  - Administer **diazepam at 0.1-0.5 mg/kg IV** (t1/2 = 15-60 min); may be repeated 2-3 times over 5-10 minutes.
  - If an intravenous line cannot be established, administer **diazepam at 0.5 mg/kg per rectum via a tomcat catheter.**

- Draw blood for CBC, glucose (stat) PCV/TP, electrolytes and biochemistry profile, and anticonvulsant levels (if patient is already current receiving medication).
- Obtain and ECG tracing from the patient

- **Patient Management Post-Diazepam**
  - If diazepam is ineffective in controlling seizures, give and anticonvulsant dose of **phenobarbital - 5mg/kg IV, and repeat every 30-40 minutes for up to 3 doses.** Phenobarbital will take approx. 20-30 minutes to reduce seizure activity.
  - If seizure clustering or status epilepticus continues, one of the following regimens may be used
    - Midazolam 0.5 mg/kg IV bolus, followed by constant rate infusion is the preferred agent to use in combination with phenobarbitone and/or propofol
    - Thiopental given as 2-4 mg/kg IV boluses to effect, up to 10-20 mg/kg, endotracheal intubation, isoflurane anesthesia. Pay attention to ventilation and circulation.
    - Propofol given as 1-2 mg/kg IV boluses to effect, followed by a CRI of propofol at 0.1-0.2 mg/kg/min IV.
    - Pentobarbital given as IV bolus of 2-6 mg/kg
    - Diazepam CRI at 1-2 mg/kg/hr in a 5% dextrose solution

NB: focal seizures can lead to life threatening hyperthermia if they are not controlled, and should be managed as for status epilepticus

- **Correction of Underlying disease and/or Secondary Effects -**
  - Metabolic acidosis - will usually correct once seizures stop and with fluid and oxygen support.
  - Hypoglycemia - treat with 0.5 g/kg of 50% dextrose, diluted to a 10% solution, and given slowly IV over 10 minutes. Avoid hyperglycemia as this may exacerbate toxic brain damage.
  - Hypocalcemia - give 15 mg/kg of 10% calcium gluconate IV slowly over 30 minutes.
  - Thiamine deficiency in cats – thiamine is administered at 2 mg/kg IM if diet or history (anorexia, treatment with antibiotic therapy, etc. suggestive of deficiency.
  - Hyperthermia - cold ice packs on trunk, inguinal, axilla regions, moist towels, cool fan. Cool body temperature to 39.5°C - hypothermia will rapidly develop if patients are actively cooled beyond this point.
  - Gastric lavage and colonic enema for ingested toxins
  - Increased intra-cranial pressure – usually the result of a structural brain disease; manage with intravenous fluid therapy, adequate ventilation strategies, followed by mannitol 1 g/kg IV PRN, furosemide 2 mg/kg IV, +/- methylprednisolone sodium phosphate 10 mg/kg IV

- **Monitoring the patient** - pay close attention to the following
  - Airway patency
  - Ventilation - SpO2, blood gases, mucus membrane color
  - Tissue perfusion - mucus membrane color, thermoregulation, blood pressure, pulse character, ECG rhythm.
  - Electrolytes, PCV/TP

- Neurological status - evidence of raised intracranial pressure, lateralizing signs, and abnormal inter-ictal signs.
- ARDS, neurogenic pulmonary edema.

Further diagnostic testing is advised for the following patients

- Animals under 1 year of age, or older than 5 years of age
- Abnormal neurologic behavior in the inter-ictal phase
- Animals with systemic disease, animals with focal seizures

Further diagnostic tests include

- Serum bile acids
- Ammonia tolerance test
- Abdominal ultrasound
- Thoracic radiographs
- CSF analysis
- Intracranial imaging (CT or MRI)

Differential Diagnosis for Status Epilepticus

primary epilepsy	secondary seizures (structural diseases of the brain)	reactive seizures (normal brain stressed by extracranial disease)
*** intrinsic chemical abnormality not associated with demonstrable intra- or extracranial disease**	Congenital * hydrocephalus * lissencephaly * storage diseases * vascular anomaly Traumatic * immediate * post-trauma Inflammatory * distemper * FIP * FeLV * Toxoplasmosis * mycosis * bacteria Neoplasia - primary or metastatic Vascular-cerebrovascular accident	Intoxication * lead * organophosphates * chlorinated hydrocarbons * metaldehyde, carbamates * strychnine, 1080 * drugs, garbage Metabolic * hypoglycemia, hypocalcemia * hyperkalemia, acidosis, alkalosis * hepatic encephalopathy * uremia * hyperlipoproteinemia Nutritional * thiamin Hypoxia * cardiovascular disease * respiratory disease * birth * anesthetic accident Hyperthermia