SEIZURES

Management – New Options
FORMULARY

- Zonisamide (Zonegran) 5-10mg/kg BID
  - 25, 50, 100mg capsules
- Levetiracetam (Keppra) 20-60mg/kg TID
  - 250mg, 500mg, 750mg
- Pregabalin (Lyrica) 2-4mg/kg BID
  - 25, 50, 75, 100, 150, 200, 225, and 300 mg capsules
- Rufinamide (Banzel) 10-20mg/kg BID
  - 200mg, 400mg tablets

- Topiramate (Topomax) 2-5mg/kg BID
  - 25, 50mg tablets
- Gabapentin (Neurontin) 10-30mg/kg T-QID
  - 100, 300, 400, 600, 800mg Capsules/tablets
FORMULARY

- Lacosamide (Vimpat) 100-200mg BID (humans)
  - 50, 100, 150, 200mg tablets
- Clobazam (Onfi) 0.5mg/kg BID?
  - 5, 10, 20mg tablets
- Stiripentol (Diacomit) 50-100mg/kg/day B-TID
  - 250, 500mg tablets, suspension

- BI Anticonvulsant.....
DON’T USE FORMULARY

- KBr – Respiratory toxic in Cats
- Lamotrigine (Lamictal) – cardiotoxic in dogs

- Verapamil – no effect
- Dilantin
- Depakote/Depakene
- Primidone
NEW SEIZURE PEARLS 2010-2012

- NCSU - ABCB1 Gene Defect – Easier to control epileptics

- Denmark - Belgian Shepherd Epilepsy Study – normal life span but epilepsy percentage of reasons for death (also 2 SUEDS).

- England – 41% of epileptics had clusters – no age, breed predilection but intact animals had more clusters

- Korea – Zonisamide 60% effective sole agent
Auburn – Seizure control - 85% pheno 52% KBr

Minnesota – Status – 60mg/kg Keppra – once significant improvement in control

England – Juvenile onset <1y seizures – 22% remission rate (humans 60%).

NCSU - The pharmacokinetics of levetiracetam in healthy dogs concurrently receiving phenobarbital. PB lowered LEV levels
- Germany - CSF Glucose – not indicative of infection – just inflammation

- TAMU – PSS surgery – pre treat with Keppra no seizures vs 4/84

- Denmark – PBGV – 9% epileptics

- England – Seizures and brain tumors - 68 dogs (42 had seizures 24 did not). Contrast enhancement, frontal lobe and herniation - risks

Penn - A novel implanted device to wirelessly record and analyze continuous intracranial canine EEG. Treat only when going to have seizure!

Germany - Add-on treatment with verapamil in pharmacoresistant canine epilepsy. – Bradycardia and hypotension – no effect
Non Epileptic Attacks

Breath Holding Episodes
Reflex Syncope
Benign Paroxysmal Vertigo
Vasovagal Attacks
Sleep Disorders
Pseudoseizures
Munchhausen Syndrome

EEG – 20% have normal EEG
Truly normal or “out of reach of electrodes”

Improve by sleep deprivation; flashing lights; hyperventilation; prolonged periods
SPOT

12 year old Chihuahua
Cluster/isolated seizures
- Meds: Phenobarbital, Kbr, gabapentin, clorazepate
- Zonisamide
Rex

9y Lab Mix

Pheno, Kbr, Lyrica, gabapentin, Zonisamide, valproic acid, acetazolamide, banzel
Generalized seizures.

Absence seizures, appear to be staring into space These seizures are sometimes referred to as petit mal seizures, which is an older term.

Tonic seizures cause stiffening of muscles of the body

Clonic seizures cause repeated jerking movements of muscles on both sides of the body.

Myoclonic seizures cause jerks or twitches of the upper body, arms, or legs.

Atonic seizures cause a loss of normal muscle tone - will fall down or may drop head involuntarily.

Tonic-clonic seizures cause a mixture of symptoms, older term: grand mal seizures.
Simple focal motor seizure

Remain conscious - sudden focal jerking of a muscle group

Complex focal seizure

Change in or loss of consciousness. Dreamlike experience. May display strange, repetitious behaviors (automatisms) such as blinks, twitches, mouth movements, walking in a circle.
60% of childhood epilepsy resolves and 60% controlled with monotherapy

60 percent of people with epilepsy have focal seizures.

These seizures are frequently described by the area of the brain in which they originate.
Bromide first used in the late 1800’s
Negative side effects made it a less than ideal medication
Discontinued in 1912 in US
Reappeared in 1980’s for veterinary use
Used in Europe for people

Phenobarbital 1912
Despite its shortcomings, phenobarbital became the main drug prescribed for epilepsy for the next 26 years.
Anticonvulsant History

Phenytoin (Dilantin) was introduced in 1938 is still a major drug used today in human seizure control.

From 1945 to 1960 a series of anticonvulsant drugs based on trimethadione (Tridione)

Diazepam 1963

Carbamazepine (Tegretol) 1974

Valproic acid (Depakene) 1978
Drugs not routinely used in veterinary medicine

Primidone

Carbamazepine (Tegretol, Carbatrol)

Phenytoin (Dilantin)

Valproic acid (Depakene)/Divalproex (Depakote)

Ethosuximide (Zarontin)/Methsuximide (Celontin)
Anticonvulsant Recent History

In the 1990’s another crop of new medications appeared.

These drugs are reported to have fewer side effects, but with similar efficacy (questionable) in the control of seizures.
When/Why to Start Treatment

- More than 1 seizure in a 4-6 week period
- Active intracranial disease (neoplasia, inflammation)
- Cluster seizures
- Status epilepticus
Clinical findings, treatment, and outcome of dogs with status epilepticus or cluster seizures: 156 cases (1990-1995).


- Underlying causes of seizures were primary epilepsy (26.8%), secondary epilepsy (35.1%), reactive epileptic seizures (6.7%), primary or secondary epilepsy with low serum antiepileptic drug concentrations (5.7%), and undetermined (25.8%).

- 186 resulted in admission to the ICU. CRI of diazepam or phenobarbital.

- Of 194 admissions, 74.7% (145) resulted in discharge from the hospital.

- 2.1% (4) in death, and 23.2% (45) in euthanasia.

- Poor outcome (death or euthanasia) was significantly associated with GME, loss of seizure control after 6 hours of hospitalization, and the development of partial status epilepticus.
MOA – MECHANISMS OF ACTION
MOA

Carboxylic acids/ Fatty acid derivatives
1. GABA transaminase inhibitor - Valproic acid
2. GABA reuptake inhibitor - Tiagabine

GABA analogs
1. Gabapentin, Pregabalin, Vigabatrin

Channel Blockers
1. Sodium
   - Fosphenytoin, Phenytoin
2. Carboxamides
   - Carbamazepine, Oxcarbazepine, Rufinamide
3. Calcium
   - Ethosuximide

Channel Openers
1. Potassium - retigabine
Unknown/ungrouped

Phenyltriazines - Lamotrigine

Oxazolidinediones Ethadione, Paramethadione, Trimethadione

Ureas – Phenacemide, Pheneturide

Monosaccharides - Topiramate
Table 2. Summary of the Mechanism of Actions of Currently Available Antiepileptic Drugs.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Decrease seizure onset</th>
<th>Enhanced GABA activated Cl-conductance</th>
<th>Reduced Ca(^{2+}) channel current</th>
<th>Decrease seizure spread</th>
<th>Novel mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenobarbital</td>
<td>++</td>
<td>+</td>
<td>?</td>
<td>?</td>
<td></td>
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<tr>
<td>Bromide</td>
<td>++*</td>
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<tr>
<td>Felbamate</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Benzodiazepines</td>
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<tr>
<td>Gabapentin</td>
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<td>Topiramate</td>
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<tr>
<td>Zonisamide</td>
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<tr>
<td>Pregabalin</td>
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<tr>
<td>Lacosamide</td>
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<td>CRMP</td>
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<tr>
<td>Rufinamide</td>
<td>++</td>
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</tbody>
</table>

*Competitive displacement of Cl- through activated GABA receptors; ? = Possible mechanism; SV2a=synaptic vesicle 2A binding; CRMP=collapsin response mediator protein 2 binding.
Felbamate (Felbatol)

Dicarbamate medication approved for use in 1993

Increases seizure threshold and prevents seizure spread by reducing excitatory neurotransmission in the brain

In dogs used as an add on for refractory seizures, not generally used as monotherapy

Felbamate (Felbatol)

Undergoes hepatic metabolism by $P_{450}$ system and is also excreted by the kidneys.

$T_{1/2}$ 5-6 hours with steady state reached in 1-2 days

Dose 15-20 mg/kg q8 hours, has been used as high as 65 mg/kg

Non sedating with a high margin of safety

Idiosyncratic aplastic anemia secondary to bone marrow suppression and liver toxicity

Similar but rare and reversible hepatotoxicity and blood dyscrasias seen in dogs

Monitoring Parameters

CBC, chemistry at 1 month after starting treatment, then q 3-6 months
Treatment of partial seizures and seizure-like activity with felbamate in six dogs.


- Six dogs with partial seizures or partial seizure-like activity

- Median duration of therapy was nine months (range two to 22 months).

- All dogs experienced a reduction in seizure frequency after felbamate administration.

- Reversible haematological adverse effects were detected in two dogs, with one dog developing concurrent keratoconjunctivitis sicca.
Gabapentin (Neurontin)

Designed to mimic GABA, but does not have similar pharmacological properties of GABA nor does it bind to GABA receptors.

Facilitates transport of GABA out of cells to act on the GABA$_A$ receptor to increase inhibitory activity and block sodium channels.

Undergoes partial hepatic metabolism, but mostly excreted by the kidneys.
Treatment with gabapentin of 11 dogs with refractory idiopathic epilepsy.

- 11 dogs with refractory idiopathic epilepsy
- All had generalised tonic-clonic seizures and had been treated with a combination of phenobarbital and potassium bromide
- Compared for the three months before and after
- **Six of the dogs showed a positive response.** minimum 50 per cent reduction in the number of seizures per week was interpreted as a positive response
- Mild side effects of ataxia and sedation were observed in five of the dogs, but they were not severe enough to warrant the treatment being discontinued during the trial.
Improving seizure control in dogs with refractory epilepsy using gabapentin as an adjunctive agent


DESIGN: 17 dogs; 16 of which have idiopathic epilepsy.

PROCEDURE: Patients were stabilised using phenobarbitone and/or potassium bromide and dosed additionally with gabapentin at 35 to 50 mg/kg/d (divided twice or three times daily) for 4 months.

RESULTS: There was no significant decrease in the number of seizures over the study period for the entire cohort, however three dogs stopped seizing completely.

• Side effects observed - sedation and hind limb ataxia.
• Long-term, a further two patients became seizure free and ten patients remained on gabapentin indefinitely. No long-term side effects have become apparent.

CONCLUSION: Addition of gabapentin increased the interictal period and shortened the post-seizure recovery in some canine epileptics. In some dogs, seizures were prevented completely, while in others there was an increase in interictal period.
Zonisamide (Zonegran)

Sulfonamide based drug that became available for use in 2000

Is used in human for treatment of focal and generalized seizures with minimal side effects

Works by blocking the propagation of epileptic discharges and suppressing focal epileptogenic activity
Zonisamide (Zonegran)

Metabolized mainly by hepatic microsomal enzymes, but **does not** induce \( \text{P}_450 \) system. \( T_{1/2} \) 15 hours

Dose 10 mg/kg q 12 hours, but if add on treatment with drugs inducing hepatic enzymes, decrease dose to 5 mg/kg q 12 hours

High margin of safety
Can be used as monotherapy

**Side effects**
- Transient sedation, ataxia, inappetance, metabolic acidosis, liver intoxication, bone marrow
- Can reduce side effects by gradually increasing the dose
- If being used with phenobarbital, recommend reducing phenobarbital dose by 25%
Zonisamide therapy for refractory idiopathic epilepsy in dogs.


Twelve dogs with poorly controlled idiopathic epilepsy were entered into a prospective, open-label, noncomparative study. Oral zonisamide was administered as an additional therapy at a dosage adequate to achieve serum drug concentrations of 10 to 40 microg/mL. Seizure frequency before and after initiation of zonisamide therapy was recorded. A dosing interval of q 12 hours was sufficient to maintain serum zonisamide concentrations within the therapeutic range.

- The mean dosage of zonisamide required was 8.9 mg/kg q 12 hours.

- Seven (58%) dogs responded favorably, experiencing a mean reduction in seizures of 81.3%.

- Five dogs had an increase in seizure frequency.

- Mild side effects (e.g., transient sedation, ataxia, vomiting) occurred in six dogs.
Prospective study of zonisamide therapy for refractory idiopathic epilepsy in dogs


- METHODS: Thirteen dogs fulfilled the inclusion criteria of poor seizure control despite adequate serum levels of phenobarbital, potassium bromide or both. One further dog was treated with zonisamide as monotherapy because of severe blood dyscrasia due to phenobarbital treatment.

- RESULTS: Data of 11 dogs could be evaluated: nine of them were responders. The median reduction of seizure frequency of all dogs on zonisamide add-on therapy was 70 per cent (range 14 to 100 per cent).

- Only transient central nervous system side effects were reported. No further increase of liver enzymes occurred. In three of the responder dogs, seizure control subsided after individual time periods (between 69 days and seven months).
Topiramate (Topamax)

Sulfamate substituted monosaccharide

Blocks seizure spread by rapidly potentiated GABA activity in the brain

In people it is used for generalized and partial seizures

In people it is primarily excreted by the kidneys unchanged

$T_{1/2}$ 20-30 hours (people), 2-4 hours (dogs), steady state reached in 1-3 days

Dose 2-10 mg/kg q 12 hours, best to start low

Side effects

GI upset, inappetence, irritability, ataxia
Levetiracetam (Keppra)

Synaptic Vesicle Protein 2 A, is required for normal nervous system functioning and is the binding site of the anti-epilepsy drug levetiracetam.

Mostly excreted unchanged in the urine, the remainder is hydrolyzed in the serum and by other organs.

No hepatic metabolism in humans or dogs.

$T_{1/2}$ 3-4 hours but may exert anticonvulsant effects that last longer than its presence in the bloodstream.

Dose 20 mg/kg q 8 hours.
The efficacy and tolerability of levetiracetam in pharmacoresistant epileptic dogs.

- Volk HA, Matiasek LA, Luján Feliu-Pascual A, Platt SR, Chandler KE.

- **8/14 dogs responded significantly** to the treatment and seizure frequency was reduced by 50%.
- In dogs that remained refractory, the dosage was increased to 20 mg/kg TID for 2 months. **One further dog** responded to levetiracetam treatment.

- Levetiracetam responders had a significant decrease in seizure frequency of 77% (7.9+/−5.2 to 1.8+/−1.7 seizures/month) and a decrease in seizure days per month of 68% (3.8+/−1.7 to 1.2+/−1.1 seizure days/month).

- However, **6/9 responders experienced an increase in seizure frequency and seizure days after 4-8 months** continuing with the levetiracetam treatment at the last effective dosage.
Levetiracetam as an adjunct to phenobarbital treatment in cats with suspected idiopathic epilepsy.


- ANIMALS: 12 cats suspected to have idiopathic epilepsy that was poorly controlled with phenobarbital or that had unacceptable adverse effects.

- PROCEDURES: Cats were treated with levetiracetam (20 mg/kg [9.1 mg/lb], PO, q 8 h).

- RESULTS:
  - Median seizure frequency prior to treatment with levetiracetam (2.1 seizures/mo) was significantly higher than median seizure frequency after initiation of levetiracetam treatment (0.42 seizures/mo).
  - 7 of 10 cats were classified as having responded.
  - Two cats had transient lethargy and inappetence.
Pregabalin (Lyrica)

- Structural analogue to GABA
- No effect on GABA receptors
- Renal excretion
- $T_{1/2}$ 6 ½ hours (people)

Current study in dogs dose
2-4 mg/kg q 12 hours
Pregabalin as an adjunct to phenobarbital, potassium bromide, or a combination of phenobarbital and potassium bromide for treatment of dogs with suspected idiopathic epilepsy.


- OBJECTIVE: Pregabalin as an adjunct to phenobarbital, potassium bromide

- ANIMALS: 11 client-owned dogs

- RESULTS: Seizures were significantly reduced (mean, 57%; median, 50%) after pregabalin administration
  - 9 dogs that completed the study; 7 were considered responders with mean and median seizure reductions of 64% and 58%, respectively.
  - Adverse effects for pregabalin were reported in 10 dogs.
**Rufinamide (BANZEL)**

- No published clinical studies in dogs
- One published pharmacokinetic study
- Dose 10-20mg/kg BID
- Clinical experience – good
Rufinamide: a new antiepileptic medication for the treatment of seizures associated with lennox-gastaut syndrome.


- **STUDY SELECTION AND DATA EXTRACTION:** Published controlled trials

- **DATA SYNTHESIS:** Rufinamide is a new antiepileptic agent that differs structurally from other antiepileptic drugs and is approved as adjunctive therapy for Lennox-Gastaut syndrome (LGS). It prolonging sodium channel inactivity, stabilizing cell membranes. It is absorbed and metabolized extensively, then excreted renally as an inactive metabolite. Clinical trials show that adjunctive rufinamide is effective at reducing seizure frequency in patients with LGS and refractory partial seizures. Rufinamide is well tolerated, causing headache, dizziness, and fatigue at rates of >10%.

- **CONCLUSIONS:** Data show that rufinamide is safe and effective as an adjunctive agent for LGS and may be used to treat partial seizures.
LACOSAMIDE (VIMPAT)

- No clinical studies in dogs
Clobazam

- Benzodiazepine (5, 10, 20mg)
- $3-4/pill
- 2.5mg/kg TID?
Stiripentol

- Initial dose is 50 mg/kg per day. This may be increased up to 100 mg/kg per day, with a maximum of 4g
- B-TID

- 250 mg, 500 mg capsules; suspension

- **Inhibits** cytochrome P450
The third-generation AEDs consist of 20 novel drugs

- brivaracetam (BRI)
- carabersat (CRB)
- carisbamate (CBM)
- DP-valproic acid (DP-VPA)
- eslicarbazepine acetate (ESL)
- fluorofelbamate (FFBM)
- fosphenytoin (FPHT)
- ganaxolone (GNX)
- lacosamide (LCM)
- losigamone (LSG)
- pregabaline (PGB)
- remacemide hydrochloride (RMC)
- retigabine (RTG)
- rufinamide (RUF)
- safinamide (SAF)
- seletracetam (SEL)
- soretolide (SRT)
- stiripentol (STP)
- talampanel (TLP)
- valrocemide (VLR)
Table 1. A new generation of existing AEDs, their parent compound and improvements.

<table>
<thead>
<tr>
<th>New compound</th>
<th>Parent AED</th>
<th>Improvement</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brivaracetam</td>
<td>Levetiracetam</td>
<td>Efficacy</td>
<td>More potent binding to SV2A</td>
</tr>
<tr>
<td>Seletracetam</td>
<td></td>
<td></td>
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<tr>
<td>Oxcarbazepine</td>
<td>Carbamazepine</td>
<td>Tolerability</td>
<td>Improved pharmacokinetic properties</td>
</tr>
<tr>
<td>Eslicarbazepine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluorofelbamate</td>
<td>Felbamate</td>
<td>Tolerability</td>
<td>Non-toxic metabolite</td>
</tr>
<tr>
<td>JZP-4</td>
<td>Lamotrigine</td>
<td>Efficacy</td>
<td>Improved pharmacokinetic properties and efficacy</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>Gabapentin</td>
<td>Efficacy</td>
<td>Equally potency to gabapentin</td>
</tr>
<tr>
<td>Valproamide, Valnoctamide, Propylisopropyl acetamide (PID), N-methyl-2,2,3,3-tetramethylcyclopropylamide (MTMCD), NPS-1776, Tetramethylcyclopropancarbonylurea (TMCU)</td>
<td>Valproate</td>
<td>Tolerability</td>
<td>Less toxic metabolites, less teratogenic potential</td>
</tr>
</tbody>
</table>
Epilepsy Surgery

- 3 drug failures
- Impaired consciousness, injury, stigmatizing behavior (disrobing, uttering obscenities), noxious auras (vomiting/fear)
- At least 1/month
- CPS and Tonic/Clonic – most common

- 50% of intractable patients have surgically remediable epilepsy

- Control after sx 58% seizure free vs 8% with continued drug management in one study

- Workup – EEG, MRI, neuropsychological evaluation.

- If not definitive then invasive EEG, nuclear med (PET, SPECT) and WADA (sodium amylobarbital) test.
• **Syndromes Amenable to Surgery:**
  - Mesial Temporal Lobe Epilepsy (hippocampus and amygdala);
  - Frontal Lobe epilepsy; Lesional Partial Epilepsy; Cryptogenic Neocortical Epilepsy

• **Surgery options**

  - Lesionectomy, lobectomy, hemispherectomy, subpial transections, corpus collosotomy

Success rates; Anterior temporal lobectomy 70% success; other areas 40-60% seizure free; CC 50-80% reduction

Deficits – some are expected. Many transient. 50% minor field of vision loss. 1-2% permanent morbidity.
ELECTROSTIMULATION PROCEDURES

Vagal Nerve Stimulations
Deep Brain Stimulation
VNS

- Does not eliminate seizures
- 27-64% reduction
Arrow points to what?
Use of vagal nerve stimulation as a treatment for refractory epilepsy in dogs.

- JAVMA 2002 Oct 1;221(7):977-83.

- **ANIMALS:** 10 dogs with poorly controlled seizures.

- **RESULTS:** No significant difference overall 13-week treatment. During the final 4 weeks of the treatment period, a significant decrease in mean seizure frequency (34.4%) was detected.

- Complications included transient bradycardia, asystole, and apnea during intraoperative device testing, and seroma formation, subcutaneous migration of the generator, and transient Horner's syndrome.
Personal Experience

- **1 DDB (Gaia)**
  - Reason: Spinal deformity and epilepsy
  - Outcome: Initially good (lowered meds); lead complication

- **1 Husky (Stoli)**
  - Severe clusters – numerous medications
  - Short lived improvement then DOA
Results of recent prospective studies of hippocampus stimulation
a) Randomized double-blind studies of the effectivity of bilateral hippocampus stimulation in 9 patients with temporal lobe epilepsy due to uni- or bilateral hippocampal sclerosis. Follow-up time: 18 months. Observed side effects were: skin erosions requiring treatment in 3 patients 24 months after implantation (data from Velasco et al. 2007 [22])
b) Open prospective studies of the efficacy of bilateral hippocampus stimulation in 10 patients with temporal lobe epilepsy, who underwent invasive monitoring. Follow-up time: 31 months. No subjective or objective side effects of treatment were observed (data from Boon et al. 2007 [25])
Hemispherectomy
Indications
Rassmusen's Encephalitis
Hemimegaloencephaly
Sturge Weber Syndrome
Skull X-Ray of Patient who had Subdural electrodes inserted for localisation of the epileptic Focus

- Functional hemispherectomy: extensive cortical resection in temporal and central cortex with disconnection of residual frontal and occipital cortex by transecting white matter fibers (not shown).
10 year old Hemimegalencephaly
Status post left hemispherectomy
Risks of Hemispherectomy

- Hemorrhage is a risk for hemispherectomy.
- Disseminated intravascular coagulation
- "Aseptic meningitis,"
- Hydrocephalus, 20–30% of patients.

- **Death from surgery - approximately 2% of patients.**
Recovery of functions after neonatal or adult hemispherectomy in cats. III. Complex functions: open field exploration, social interactions, maze and holeboard performances.

- Burgess JW, Villablanca JR, Levine MS.

Complex behavioral patterns were studied in cats with removal of the entire left cerebral hemisphere
- neonates (n = 10) or adults (n = 11); control (n=24)

- Adult cats showed decreased open field activity in locomotion, rearing and sniffing.
- Kittens showed similar deficits at 100 days of age
  - by 150 days of age they resembled normal littermates in all 3 measures.
Recovery of function after neonatal or adult hemispherectomy in cats:

- Villablanca JR, Burgess JW, Olmstead CE.

Cats with removal of the left hemitelencephalon (hemispherectomy) as neonates (n = 12) or in adulthood (n = 14), were compared using a battery of 16 neurological and behavioral tests given when they were young adults (kittens) or at least 5 months after the lesion (adults).

The neonatal-lesioned subjects grew normally and performed markedly and significantly better than adult-lesioned cats.

- None of the animals recovered tactile placing of the right forelimb or a normal vision in the right visual field.
- Overall recovery was outstanding for all cats.
- Neonatal-lesioned were hard to differentiate from intact controls in their spontaneous, daily activities.
Operative technics and principles utilized in total hemispherectomy in the monkey and the dog.

WHITE RJ, MACCARTY CS, GRINDLAY JH, SCHREINER LH.
Absence of temporal lobe epilepsy pathology in dogs with medically intractable epilepsy.

- Buckmaster PS, Smith MO, Buckmaster CL, LeCouteur RA, Dudek FE.
- Department of Comparative Medicine, Stanford University School of Medicine, CA

Temporal lobe epilepsy is the most common type of epilepsy in adult humans, it is frequently resistant to anticonvulsant therapy.

We sought to test the hypothesis that dogs with medically intractable epilepsy have temporal lobe epilepsy. The hippocampi of 6 dogs that were euthanized because of chronic, recurrent seizures were compared with those of 8 nonepileptic controls.

These findings demonstrate a lack of hilar neuron loss and granule cell axon reorganization, suggesting that temporal lobe epilepsy is not a common cause of medically intractable epilepsy in dogs.
Callosotomy

- Rougier A, Claverie B, Pedespan JM, Marchal C, Loiseau P. Clinique Universitaire de Neurochirurgie, Hôpital Pellegrin-Tripode, Bordeaux, France.

- **Atonic and tonic astatic seizures** characterized both by clinical and electroencephalographical specific patterns, are the most responsive.
- > 50% reduction in seizure frequency to a complete cessation, in 60 to 80% of the patients.

- For **tonic-clonic seizures**, favorable outcome fluctuates from 40% to 80% principally according to the extension of the section.

- **Other types of seizures are not indicated** for callosotomy even though some improvement may be observed.
Multiple Subpial Transections
**Young Dog - Healthy**

- Phenobarbital
- Potassium bromide
- Zonisamide
- Levetiracetam
OLD DOG STRUCTURAL PROBLEM

- Levetiracetam (Keppra) or zonisamide (Zonegran)
- Felbamate (Felbatol)
**Liver Disease**

- Levetiracetam (Keppra) or Potassium Bromide
- Gabapentin (Neurontin)
- Pregabalin (Lyrica)
- Topiramate (Topimax)
Refractory Combos

- Phenobarbital and levetiracetam
- Phenobarbital and KBr (side effects)
- Zonisamide and KBr
- Zonisamide and levetiracetam
- Phenobarbital and zonisamide (double zonisamide)
Severely Refractory Refer?

- Rufinamide/Banzel
- Lacosamide
- Clobazam
- Surgery
QUESTIONS?
CASES?