Acute Spinal Cord Injury:
Pathophysiology and treatment

Natasha Olby Vet MB, PhD, DACVIM (Neurology)
NCSU CVM, Raleigh, NC
The task I must undertake is towering over me like a great big monolith

It is too big to contemplate, so I think I will go and have a little look at the internet
Outline

- Pathophysiology of acute spinal cord injury
- Treatment options for contusive and ischaemic injury
- Disc disease: summary of some of the literature
- Surgical therapy of disc disease
- Ideas about chronic paralysis
Most common causes of SCI: Intervertebral Disc Disease (IVDD)
Pathological events occurring

- Compression
- Contusion
Most common causes of SCI
Fibrocartilagenous Emboli (FCE)
Most common causes of SCI: Trauma
Pathological events occurring

※ Laceration
※ Compression
※ Contusion
Medical challenges for us

- Can we prevent or limit the extent of injury?
- Can we restore motor function if we fail in our first endeavor? (i.e. they become paralyzed?)
Do we understand the spinal cord?
Do we understand the spinal cord?

- 10 year old hound dog
- Acute onset of paraplegia,
  - owners were sure it was normal prior to this

- 14 m Irish Wolfhound
- Ambulatory paraparetic
Anatomy: the spinal cord

WM damage: profound consequences caudally
Anatomy: the spinal cord

GM damage: profound consequences at the level of the damaged spinal cord segments
Anatomy: the arterial supply

- Segmental spinal arteries divide into dorsal and ventral radicular arteries that then supply the dorsolateral & ventral spinal arteries.

Note the ventral GM is supplied by the ventral spinal artery alone.
Anatomy: the venous drainage

- Venous drainage
  - Parenchymal veins drain to the......
  - Internal vertebral venous plexus
Anatomy: the blood supply

* Veins are compressed more easily than arteries
* Venous pressure is approximately 2 - 3 mmHg higher than CSF pressure and is closely linked to CSF pressure
* *Spinal cord perfusion pressure is dependent on*
  * Arterial blood pressure
  * CSF pressure (~ venous pressure)
Physiology: the blood supply

- Spinal cord blood flow is dependent on:
  - perfusion pressure
  - vascular resistance
  - viscosity

- Spinal cord perfusion pressure is dependent on:
  - Arterial blood pressure
  - CSF pressure

SCPP = ABP - CSFP

SCPP: spinal cord perfusion P
ABP: arterial blood pressure
CSF: cerebrospinal fluid
Physiology: the blood supply

- Blood flow is autoregulated by changing vascular resistance
  - Pressure autoregulation
  - Chemical autoregulation
- Blood flow remains constant until perfusion pressure drops below 50mmHg due to these autoregulatory mechanisms (Griffiths et al., 1978)
- Autoregulation fails in the injured spinal cord

- Spinocord blood flow is dependent on
  - perfusion pressure
  - vascular resistance
  - viscosity
Pathophysiology

* Majority of information is derived from rodent models of SCI “weight drop model”
* We rarely see an equivalent injury type in clinical practice
Contusive injury

- Primary mechanical damage
- Secondary tissue destruction
  - Acute phase 24 - 48 hours
  - Subacute phase – days to months
  - Chronic phase – months to years

Vascular injury
Acute traumatic injury

Direct parenchymal & vascular injury
Acute traumatic injury

Direct parenchymal & vascular injury

Haemorrhage

Ischaemia

NT release

Energy failure

Mitochondrial failure

Activation of
- Proteases
- Lipoprotein A
- Caspase
- Calpain

Excitotoxicity

↑ Na⁺; Ca ++

Free radical production

Inflammatory mediators

Necrosis

Apoptosis
Acute traumatic injury

Direct parenchymal & vascular injury

Haemorrhage

Ischaemia

NT release

Energy failure

Mitochondrial failure
Activation of
- Proteases
- Lipoprotein A
- Caspase
- Calpain

Free radical production

Inflammatory mediators

Excitotoxicity
Na⁺; Ca ++

Necrosis Apoptosis
Excitatory amino acids

Syntichaki & Tavernarakis
Excitatory amino acids

Energy failure results in failure of

Excitotoxicity

Pertinent to dogs
Contusive/vascular injuries: early consequences of Na influx

Corticosteroids will not affect this edema
- It is intracellular
- Due to increased sodium concentrations
Consequences of calcium influx

- Calpain
- Caspase
- Phospholipase A2
- Binds phosphates
- Necrosis
- Apoptosis
- Eicosanoids
- Further depletes energy
## Therapy of ion fluxes

<table>
<thead>
<tr>
<th></th>
<th>Nimodipine, nifedipine</th>
<th>Riluzole</th>
<th>MK801, NBQX</th>
<th>Gacyclidine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of action</strong></td>
<td>Ca channel antagonist</td>
<td>Na channel antagonist</td>
<td>NMDA/AMP A antagonists</td>
<td>NMDA antagonist</td>
</tr>
<tr>
<td><strong>Clinical efficacy</strong></td>
<td>No</td>
<td>Phase 2/3 human trial ongoing</td>
<td>Too many adverse effects</td>
<td>Safe but no efficacy</td>
</tr>
</tbody>
</table>
Reactive Oxygen Species

* ROS (free radicals): peak within 12 hours

- Lipid peroxidation
- Nitrate & oxidate
- Target mitochondrial enzymes
- Membrane damage
- Protein & nucleic acid damage
- Inhibit mitochondrial respiration
Reactive nitrogen species

Nitrite + superoxide $\rightarrow$ Peroxynitrite

- Peroxynitrite is now believed to play an important role in mitochondrial dysfunction
- Interest is focusing on mechanisms of attenuating PN damage – tempol and uric acid
Therapy of ROS: MPSS

- NASCIS trials suggested efficacy
  - Free radical scavenger when used at 30mg/kg bolus then 5.4mg/kg/h for 24-48 h
  - Only if within 8h of injury

- Much controversy over these results

- Has been evaluated in a canine multicenter randomized, placebo controlled, blinded, prospective clinical trial

Efficacy not demonstrated in our hands
Therapy of ROS: N-Acetylcysteine

Clinical trial in 70 dogs with acute disc herniations

No benefit detected

- Long window to therapy
- Dogs had a range of injury severities
- Poor penetrance of the drug was suspected
ROSS: DMSO

ROS: DMSO

Efficacy of a Metalloproteinase Inhibitor in Spinal Cord Injured Dogs


- No difference in dogs with incomplete lesions
- Dogs with complete lesions did significantly better with DMSO
- BUT – only 6 – 7 dogs per treatment group
  - Control group showed no recovery.....more in next lecture!
Polyethylene Glycol

- Surfactant
- Fusogen
Direct parenchymal & vascular injury

Acute traumatic injury

Haemorrhage
Ischaemia
NT release

Free radical production
Inflammatory mediators

Energy failure
Mitochondrial failure
Activation of
- Proteases
- Lipoprotein A
- Caspase
- Calpain

Excitotoxicity
$Na^+; Ca^{++}$

Necrosis
Apoptosis
polyethylene glycol

PEG, 3500 Dalton, 30% w/w in saline: filter it

2ml/kg at time zero and then repeat at 45 minutes

~68% treated dogs recovered, 25% of historical untreated dogs did not
Deep pain negative disc dogs
Within 24 hours of paralysis
All had decompressive surgery

Placebo
MPSS
PEG

Weeks 1-4
Weeks 5-8
Weeks 9-12

Efficacy not demonstrated in our hands
Other promising drugs, not yet evaluated in dogs

- Multiple possible mechanisms of action
- Minocycline — *phase 2 human trial did not show significant improvement but positive trends* (Casha et al, 2012)
- Erythropoietin — *Protective cytokine; no human clinical trial*
- Cyclosporine A/Tacrolimus — *human trials in Europe?*
- Melatonin — *no human clinical trial yet*
- Hypothermia — *lots of experimental evidence....phase 1 clinical trials completed in people*
- GGF2 — *trial ongoing*
- Calorie restriction — *only 1 experimental paper but intriguing*
Acute traumatic injury

- Direct parenchymal & vascular injury
  - Haemorrhage
  - Ischaemia
  - NT release

Energy failure

- Mitochondrial failure
  - Activation of
    - Proteases
    - Lipoprotein A
    - Caspase
    - Calpain

Inflammatory mediators

Free radical production

Excitotoxicity $\text{Na}^+; \text{Ca}^{++}$

Necrosis

Apoptosis
Spinal cord perfusion: in dogs

- There is a rapid decrease (to zero) in GM perfusion (Griffiths, 1976)
- WM perfusion is maintained for longer
- Correlates to severity of injury
- In vivo measurements with US are emerging (Forterre et al)
Spinal cord perfusion: histopathology

- Destruction of the microvascular bed
- Petechial and larger hemorrhages form
Microvascular bed

Free radicals

Inflammatory mediators

Endothelial damage, vasospasm

Neurotransmitters (eg opioids)

Haemorrhage

Thrombosis

Ischaemia
Endothelial cell death

De novo expression of Trpm4 initiates secondary hemorrhage in spinal cord injury

Volodymyr Gerzanich¹, S Kyoong Woo¹, Rudi Vennekens², Orest Tsymbalyuk¹, Svetlana Ivanova¹, Alexander Ivanov¹, Zhihua Geng¹, Zheng Chen¹, Bernd Nilius², Veit Flockerzi³, Marc Freichel³ & J Marc Simard¹,⁴,⁵
Transient receptor potential channels

- Trpm4 channels – permeable to monovalent cations
- Low level of expression in the CNS
- Dramatically upregulated in endothelial cells within 24 hours of injury in rats
- We have just demonstrated the same phenomenon in dogs

Gerzanich et al., 2009
Transient receptor potential channels

- Allows rapid entry of Na$^+$ into endothelial cells

- Oncotic swelling
- Endothelial cell death
- Petechial haemorrhages
- Haem
- Ischaemia
- Increased interstitial pressure
Transient receptor potential channels

* Block Trpm expression with antisense oligonucleotide
Factors affecting spinal cord perfusion

- Direct damage to blood vessels
- Secondary damage to vessels due to neurotransmitters, inflammatory mediators, Trpm4 expression and free radicals

- Measure BP and treat hypotension
- Measure $\text{PaO}_2$ and treat hypoxemia
  - Decompress the spinal cord
Do we have any evidence of the clinical importance of perfusion?

- Significant perioperative hypotension associated with a 23 fold increase risk of major adverse event
- May transiently or permanently affect outcome
Durotomy as a means of restoring perfusion

* Most effective way to improve outcome in TBI is to maintain perfusion
* Removing CSF/reducing ICP

Unable to demonstrate maintained perfusion with durotomy

Retrospective studies do not show benefit with durotomy

*(Loughin et al 2005)*
What can we conclude?

Drug interventions have been low yield

Neuroprotective strategies

Systemic stabilization
Decompression

* The Neuroprotection group (Denmark...)*
Acute intervertebral disc disease

Natasha Olby Vet MB, PhD, DACVIM (Neurology)
NCSU CVM, Raleigh, NC
The Intervertebral Disk

- Annulus fibrosus
  - Outer, inner and transitional zones
- Nucleus pulposus
- Cartilagenous endplates

Great reviews by Bray and Burbidge, 1998 (JAHAA); Coates 2000 (Vet Clins)

Canine Neurology
Hoerlein, 1966
The beginning....

**The first report –**
- Janson 1881
- Endochondroma of the L4/5 disc

**Later reports**
- Tillmans (1939)
- Described 2 types of disk herniation – focal (Dachshund) and multifocal (old dogs)

*Canine Neurology Hoerlein, 1966*
A PATHOLOGIC-ANATOMICAL STUDY
ON DISC DEGENERATION IN DOG

With special reference to the so-called enhondrosis intervertebralis

BY
HANS-JÖRGEN HANSEN
**Disk Degeneration**

- **Chondrodystrophoid breeds** (hypochondrodysplastic)
  - Chondroid metaplasia of the nucleus
  - Cells replaced by chondrocytes
  - By 1 year 75-100% of discs contain fibrocartilage
  - Decrease in GAGs (H$_2$O), increase in collagen
  - Cellular death in nucleus – calcification
  - Secondary changes to annulus, articular facets, ligaments etc

_Hansen, 1951_
Disk Degeneration

- Nonchondrodystrophoid breeds
  - Fibroid metaplasia
  - Fragmentation and disorganization of the lamellae – fissures
  - Dehydration and loss of GAGs
  - Increased mitotic activity of fibroblasts – production of collagen
  - Lose borders between NP and TZ

Hansen, 1951
Hansen Type I disk herniation

- Described in chondrodystrophophoid dogs
- Peak incidence: 3 – 6 y (range 1 – 14y)
- 75% TL herniations between $T_{11/12}$ and $L_{1/2}$
- Also common in the Ce spine
Hansen Type I disk herniation

- Nucleus undergoes degeneration
- Develop separation and tears in the

Bray & Burbidge, 1998
Berit Funquist

- Described the ‘ascending syndrome’
- Assessed dogs differently to nowadays
  - Nociception assessed by skin pinch only
  - A lot of emphasis on the ‘tonus’ of the limbs and the presence or absence of hyper-reflexia
  - Also focused on duration of signs
Published spinal cord pathology in 23 dogs

- **Compression**
  - Wallerian degeneration
  - Demyelination
  - Vascular neogenesis

- **Malacia**
  - Little evidence of compression

- **Diffuse demyelination**
  - Often in combination with malacia
The Dachshund
The Dachshund

- Occurrence of 19% across dachshunds, some families as high as 75% (Ball et al., 1982)
- Ruled out simple trait (Ball et al., 1982)
- Complex trait, more maternal influence, environmental factors important

Disc calcification → Disc herniation

Stigen, 1996
Heritability of disk calcification

* Jensen and Christensen (2000)

- Linked chondroid metaplasia to hypochondroplasia trait *(FGF3 mutations)*
- Radiographed parents & offspring (24-35m)
- Scored calcified disks on different scales
- Performed Chi squared analysis to look at heritability
- Heritability estimate of 0.47 – 0.87
Jensen & Arnbjerg (2001)

- Longitudinal radiographic study
- 40 dogs @ 6 – 24 m, 12 dogs @ 3 to 4 years
- Site not associated with risk of calcification
- Calcified disks disappear with age
  - 4 of 12 dogs with no clinical signs of IVDD
- Max no of disks calcified at 24 – 27 m (80% dogs)
- Recommend screening at 24-48 m – adopted by Danish DS
  - Advise not to breed if >5 calcified discs
Genome-Wide Association Study in Dachshund: Identification of a Major Locus Affecting Intervertebral Disc Calcification

Mette Sloth Mogensen, Peter Karlskov-Mortensen, Helle Friis Proschowsky, Frode Lingaas, Anu Lappalainen, Hannes Lohi, Vibeke Frøkjær Jensen, and Merete Fredholm

Validation of genome-wide intervertebral disk calcification associations in Dachshund and further investigation of the chromosome 12 susceptibility locus

Mette Sloth Mogensen¹, Karsten Scheibye-Alsing¹, Peter Karlskov-Mortensen¹, Helle Friis Proschowsky¹, Vibeke Frøkjær Jensen², Mads Bak³, Niels Tommerup³, Haja N. Kadarmideen¹ and Merete Fredholm¹ *

¹ Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark
² National Food Institute, Technical University of Denmark, Lyngby, Denmark
³ Faculty of Health Sciences, Department of Cellular and Molecular Medicine, Wilhelm Johannsen Centre for Functional Genome Research, University of Copenhagen, Copenhagen N, Denmark
So what do we know of genetic cause?

- Danish work only applies to Wire Haired Danish Dachshunds
- Doesn’t identify a biologically relevant cause
- In beagles, Runx2 expression correlates to disc aging
- ......it will likely be complex
Environmental Factors

- Moderate stair climbing & increased duration of exercise were associated with decreased disk calcification.
- Body dimensions were not associated with disk calcification.
Environmental Factors

- Herniations do occur in certain locations

- Longer dogs had less chance of disc herniation

- Shorter dogs had more chance

- Logistic regression modeling is somewhat contradictory
Other breeds

Not specific to chondrodystrophoid dogs.

Large breeds tend to have a single mineralized disc (Cudia and Duval, 1997).

Many toy breeds never have disk calcification: body size related to IGF
French Bulldogs

A Comparison of Thoracolumbar Intervertebral Disc Extrusion in French Bulldogs and Dachshunds and Association With Congenital Vertebral Anomalies

Takeshi Aikawa¹,², BVSc, Diplomate JCVS, Mitsuhiro Shibata¹, BVSc, Moe Asano¹, BVSc, Yasushi Hara², DVM, PhD, Charter Diplomate JCVS, Masahiro Tagawa², DVM, PhD, Charter Diplomate JCVS, and Hiromitsu Orima², DVM, PhD

¹ Aikawa Veterinary Medical Center, Shinjyuku-ku, Tokyo, Japan and ² Nippon Veterinary and Life Science University, Kyouan-cho, Musashino-shi, Tokyo, Japan

<table>
<thead>
<tr>
<th>Grade</th>
<th>MD* (%)</th>
<th>FB† (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 (0.1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>2</td>
<td>213 (31.7)</td>
<td>15 (31.9)</td>
</tr>
<tr>
<td>3</td>
<td>209 (31.2)</td>
<td>14 (29.8)</td>
</tr>
<tr>
<td>4</td>
<td>67 (10.0)</td>
<td>3 (6.4)</td>
</tr>
<tr>
<td>5</td>
<td>181 (27.0)</td>
<td>15 (31.9)</td>
</tr>
<tr>
<td>Total</td>
<td>671</td>
<td>47</td>
</tr>
</tbody>
</table>

*Miniature Dachshund.
†French Bulldog.
Other findings

- French bulldog disc herniations not occurring at sites of malformations
- Tend to occur slightly further caudal in the spine
- 50% L1/2 – L4/5 vs 30% in Dachshunds
- More likely to develop AMM: 33% of grade 5 dogs vs 11%
Type I Disk Herniation

* Certain breeds have certain presentations

Cocker spaniels & fat old cats caudal L spine

Sha peis: cervical spine
Other Acute Disk Herniations

- Low volume, high velocity; missile; ‘type 3’
Other Acute Disk Herniations

- Can be traumatic............
Other Acute Disk Herniations

- Large breed acute annular disc herniations
- Complicated by hemorrhage
Beware of dogs with bleeding disorders

- BMBT not reliable for von Willebrands
Other Acute Disk Herniations

- Acute herniation of dehydrated, fibrotic nucleus: the old dachshund, large breeds
- Undergone chondroid metaplasia but not degeneration and calcification?
Other Acute Disk Herniations

- Acute herniation of hydrated nucleus
- Most common in the cervical spine
- Don’t forget the ‘discal cyst’
Conservative Therapy

- Detailed data on 271 dogs, Funquist, 1962
- Rest
- Vitamin B-complex
- Iodinated casein (?)
- Irgapyrine/butazolidine
- Cystitis – antibiotics and chemotherapy (!)

Intervertebral disc protrusion in the dog Pettit, 1966 (Hansen)
Current clinical scoring method

✿ 0: normal
✿ 1: Paraspinal pain, no neuro deficits
✿ 2: Ambulatory paraparesis, ataxia
✿ 3: Non-ambulatory paraparesis
✿ 4: Paraplegia
✿ 5: Paraplegia with no nociception
Conservative Therapy

Funquist outcomes

* Nonambulatory paraparetic (grade 3): n=33
  * 82% recovered, 33% ‘normal’, 49% paretic

* Paraplegic with tonus (grade 4 or 5): n=64
  * 39% recovered, (15% ‘normal’), 61% euthanized, 2% developed AMM

* Paraplegic without tonus (grade 5): n=44
  * 0% recovered, 100% euthanized, 41% developed AMM
Conservative Therapy: outcomes

* Comparison with Davies and Sharp, 1983

<table>
<thead>
<tr>
<th>Grade</th>
<th>3</th>
<th>4 (5)</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Funquist</td>
<td>82% (33)</td>
<td>39% (64)</td>
<td>0% (44)</td>
</tr>
<tr>
<td>Davies and Sharp</td>
<td>100% (10)</td>
<td>50% (6)</td>
<td>7% (14)</td>
</tr>
</tbody>
</table>

• Recurrence in 48% dogs (Funquist)
Conservative Therapy: outcomes

Evaluation of the Success of Medical Management for Presumptive Thoracolumbar Intervertebral Disk Herniation in Dogs

JONATHAN M. LEVINE, DVM, Diplomate ACVIM (Neurology), GWENDOLYN J. LEVINE, DVM, SCOTT I. JOHNSON, DVM, Diplomate ACVECC, SHARON C. KERWIN, DVM, MS, Diplomate ACVS, BIANCA F. HETTLICH, T. Diplomate ACVS, and GEOFFREY T. FOSGATE, DVM, PhD, Diplomate ACVPM

* 223 dogs (presumptive diagnoses)
* Client questionnaire driven study
* 83% ambulatory at presentation
  * 54.7% had successful outcome
  * 30.9% recurrence
  * 14.4% failure
Conservative Therapy: outcomes

- Use of steroids associated with failure
- Duration of rest not associated with outcome
Conservative Therapy of Ce discs

- 49% recovered, **33% recurrence**
- 18% failed to recover
- NSAIDs helped, duration of cage rest and steroids did not
Conservative Therapy of Ce discs

- Presumptive diagnoses from ERs and TAMU
- Telephone/questionnaire followup
- Included some unusual breeds – eg Great Dane
- Unlikely to be assessing purely type I IVDD
Fenestration alone

- Funquist 1962 – perfected a part surgical, part blind approach
- Pleural tears
- Spinal cord injury
- Hemorrhage

Textbook of Small Animal Surgery, Slatter
Fenestration by partial percutaneous discectomy

- Kinzel et al., 2005
- Placed a K wire then made the core with a 5mm Mitchel Trephine
## Fenestration alone: success rates

<table>
<thead>
<tr>
<th>Grade</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Funquist</td>
<td>93% (42)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Davies &amp; Sharp</td>
<td>85% (47)</td>
<td>94% (18)</td>
<td>33% (6)</td>
</tr>
<tr>
<td>Kinzel et al.</td>
<td>88.8% (159)</td>
<td>88.8% (159)</td>
<td>38.2% (58)</td>
</tr>
<tr>
<td>Butterworth &amp; Denny</td>
<td></td>
<td></td>
<td>33%</td>
</tr>
</tbody>
</table>

- Recurrence occurred in 48% conservatively treated dogs and 0.6 - 17% of fenestrated dogs.
Fenestration by laser

- 270 dogs with history of recovering from disc disease.
- **3.4% recurrence**, 1 developed disko, 1 needed a hemilaminectomy.
Chemonucleolysis

- Chymopapain, collagenase, hyaluronidase, chondroitinase and calpain 1.
- Do effectively digest the disc – nucleus
- Can cause too much damage
Any Questions
Surgical Treatment Acute of Intervertebral Disk Herniations

Natasha Olby Vet MB, PhD, MRCVS
Dip ACVIM (Neurology)
NCSU College of Veterinary Medicine
Questions

- Is surgical treatment of IVDD indicated?
- If so, which surgery?
History of Back Surgery

- Early skepticism that it could be done
- Fenestrations were popular
- Dorsal laminectomies - type A

Funquist & Shantz, 1962

3 mo post op
History of Surgery

- Modification of A to inject paraffin wax under the cord
- Laminectomy membrane resulted in recurrence of paralysis @ 4 weeks

Funquist and Shantz, 1962
History of Surgery

* Laminectomy Type B

7 mo post operatively

Fig. 2. Laminectomy with retention of the outer compact bone of the dorsolateral portion of the arch (technique B). From Funkquist and Schantz. Acta Orthop. Scand., Suppl. 56, 1962.

Funquist, 1962
### Funquist outcomes

<table>
<thead>
<tr>
<th>Grade</th>
<th>3</th>
<th>4/5</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Funquist A</td>
<td>82% (11)</td>
<td>35% (20)</td>
<td>60% (5)</td>
</tr>
<tr>
<td>Funquist B</td>
<td>87.5% (16)</td>
<td>78.6% (14)</td>
<td>66.7% (3)</td>
</tr>
</tbody>
</table>

*Conservative management*

<table>
<thead>
<tr>
<th>Grade</th>
<th>3</th>
<th>4/5</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Funquist</td>
<td>82% (33)</td>
<td>39% (64)</td>
<td>0% (44)</td>
</tr>
<tr>
<td>Davies and Sharp</td>
<td>100% (10)</td>
<td>50% (6)</td>
<td>7% (14)</td>
</tr>
</tbody>
</table>
Additional Funquist observations

- Noted level of recovery following conservative management
  - More dogs had an incomplete recovery when compared with surgical management
  - Recurrence was more common

Need a head to head comparison of medical vs surgical management of dogs with grade 2 or 3 injuries
Current surgical treatment of IVDD

- Aim is to decompress the spinal cord
  - Dorsal laminectomy (cervical)
  - Ventral slot (cervical)
  - Hemilaminectomy
  - Pediculectomy
  - Foramenotomy
  - Lateral corpectomy
  - Fenestration

Wheeler and Sharp
Which surgical approach?

* Hemilaminectomy
  * Great access laterally and ventrally
  * Minimal laminectomy membrane problems
Hemilaminectomy problems

- Access to contralateral side limited
- Access ventrally is limited if disc is firm/adherent
- Can cause instability/subluxation
  - If performed bilaterally
  - Certain breeds and locations (pugs, T10/11/12)
Mini-Hemilaminectomy
Pediculectomy, Foramenotomy

* Preserves articular facets
  * Dorsal limit – dorsal aspect of accessory process

* Can be performed bilaterally

Described by Bitetto and Thacher, 1987
Drawbacks

- Less access to the vertebral canal and therefore the disc material.
Lateral Corpectomy

- Moissonier et al., 2004
  - Intended for type II discs
  - Any chronic protrusion
  - 15 dogs, 7 large breed, 8 chondrodystrophoid
  - Signs for > 3wks
  - None worsened
  - All improved

Neurologic Outcome After Thoracolumbar Partial Lateral Corpectomy for Intervertebral Disc Disease in 72 Dogs

Florian Salger, Med Vet, Luisa Ziegler, Med Vet, Dr. Irene Christine Böttcher, Med Vet, Diplomate ECVN, Prof. Dr. Gerhard Oechtering, Med Vet, Diplomate ECVA, Prof. Dr. Peter Böttcher, Med Vet, Diplomate ECVS, and Dr. Thomas Flegel, Med Vet, Diplomate ACVIM (Neurology) & ECVN

Department of Small Animal Medicine, University of Leipzig, Leipzig, Germany
Other surgical approaches

- LS spine - dorsal or sometimes a dorso lateral approach
Cervical spine

- Cervical spine - ventral, dorsal or hemi
Durotomy or no durotomy?

- Theoretically decreases CSF pressure and therefore improves perfusion
- Some people use it as a diagnostic procedure
- Studies have failed to show a benefit
- I do a durotomy if the cord looks swollen to aid in decompression
Durotomy or no durotomy?

- Not completely benign procedure
**Fenestration or no fenestration?**

<table>
<thead>
<tr>
<th>Author</th>
<th>C</th>
<th>F</th>
<th>F &amp; D</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Funquist</td>
<td>48%</td>
<td>17%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levine</td>
<td>30.9%</td>
<td></td>
<td></td>
<td>4.8%</td>
</tr>
<tr>
<td>Brisson</td>
<td></td>
<td></td>
<td>4.8%</td>
<td></td>
</tr>
<tr>
<td>Mayhew</td>
<td></td>
<td></td>
<td></td>
<td>19.2-50%</td>
</tr>
<tr>
<td>Dhupa</td>
<td></td>
<td></td>
<td>6.4%</td>
<td></td>
</tr>
</tbody>
</table>

- Risk increases with no of calcified discs – 50% chance of recurrence with 5 calcified disks (Mayhew et al, 2004)
- Early recurrence – same site, late recurrence, different site (Dhupa et al, 1999)

C: conservative, F: fenestration D: decompression
Fenestration or no fenestration?

- MRIs pre op, post op & at 6 weeks
- 9 dogs fenestrated, 10 dogs not

- 0 recurrence
- 6/10 MRI recurrence
- 3/10 clinical recurrence

Influence of Intervertebral Disc Fenestration at the Herniation Site in Association with Hemilaminectomy on Recurrence in Chondrodystrophic Dogs with Thoracolumbar Disc Disease: A Prospective MRI Study

FRANCK FORTERRE, DVM, Diplomate ECVS, MARTIN KONAR, DVM, Diplomate ECVDI, DAVID SPRENG, DVM, Diplomate ECVS and ACVECC, ANDRE JAGGY, DVM, Diplomate ECYN, and JOHANN LANG, DVM, Diplomate ECVDI

Veterinary Surgery
37:399-405, 2008
Fenestration facts

- 50% owners opt for euthanasia rather than a second surgery (Mayhew et al, 2004)
- Calcified disks increase risk of recurrence (Mayhew et al, 2004)
- Fenestration technique affects recurrence

Fenestrate calcified disks
Fenestrate higher risk disks
T11/12 – L2/3
What can go wrong?

- Cut the wrong site

Always have imaging in surgery
Always double check before removing bone
Watch out for congenital anomalies
What can go wrong?

* Recurrence

Fenestrate (properly)
What can go wrong - cervical

∗ Iatrogenic damage to the spinal cord
∗ Failure to remove disk material
∗ Hemorrhage
∗ Arrhythmias
∗ Damage to local soft tissues
∗ Instability
What else can go wrong?

- Hemorrhage/hematoma
- Iatrogenic cord damage
- Instrument breakage
- Cord herniation
- Laminectomy membrane
- Instability
- Seroma formation
- FCE?
FCE - Associated with fenestration?
There is no such thing as a straightforward back.

Always investigate dogs that are not improving as expected.
Outcomes: TL discs

- Too many papers to count – dating from 1960s to now

<table>
<thead>
<tr>
<th>Grade</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Summary</td>
<td>~ 100%</td>
<td>80-100%</td>
<td>0-75%</td>
</tr>
</tbody>
</table>
Outcomes from cervical IVDD

- 100% should improve
  - Persistent neck pain – re-image if not improving
  - Need for ventilation if hypoventilating
Prospective study of 88 dogs: 4 groups, evaluated at 2, 4, 12 wks

- Group 1: initial score of 0 (plegic no sensory)
- Group 2: initial score 0.5-1 (plegic + sensory)
- Group 3: initial score 2-5 (non-ambulatory paretic)
- Group 4: initial score >6 (weight bearing VM)
Group 1: grade 5: plegic, no nociception

12 weeks: Median score: 9.5 Range 0-13
Grades 3 and 4

12 weeks: Median score: 11.25 Range 8.75-14
Median score: 12 Range 9.25-14
Recovery: Stepping Score

- Group A
- Group B
- Group C
Factors affecting outcome of dogs with nociception

- **Speed of onset of signs** (Ferreira et al, 2002)
  - Faster onset, worse outcome but no effect on speed of recovery
  - Other groups could not show this

- **Duration of signs** (Ferreira et al, 2002)
  - No effect on outcome but did influence the speed of recovery
  - Other groups could not show this

- **Disk space involved** – no effect on outcome (Ruddle et al, 2006)
Post operative laser therapy?

Low-level laser therapy reduces time to ambulation in dogs after hemilaminectomy: a preliminary study

W. E. Draper, T. A. Schubert, R. M. Clemmons and S. A. Miles

Department of Small Animal Clinical Sciences, College of Veterinary Medicine, University of Florida, Gainesville, FL, USA

* Showed decreased time to walking
Grade 5, nociception negative dogs
0-75% re-evaluated

- Scott and McKee, 1999: 34 dogs: 62%
- Olby et al, 2003: 64 dogs: 58% regained nociception and walking, 69% regained walking
- Loughin et al 2005: 81 dogs: 61% (reported as 73% but excluded dogs euthanized on the table)
- Olby et al: 2014: 64 dogs, multicenter: 48% at 12 weeks
Prognostic indicators for nociception negative dogs

- Parameters that have failed to be more useful acute prognostic tools than clinical signs
  - SEPs (Poncelet et al., 1993)
  - EIP (Poncelet et al., 1998)
  - CSF glutamate levels (Olby et al., 1999)
  - CSF MBP levels (Levine et al., 2010)
  - Spinal cord blood flow: due to technical difficulties: this needs to be re-evaluated (Olby, unpublished data)
Prognostic indicators for Grade 5 dogs

**Signs**
- Peracute onset of signs – worse prognosis (Scott et al., 1999)
- Time to surgery - > 48 hrs worse prognosis (Loughin et al 2005)

**CSF**
- Macrophage count: >13% macrophages 100% sensitive, 83% specific (Srugo et al 2011)
- CSF CK and MBP improved sensitivity over MBP alone (Wittsberger et al 2012)
- CSF c Tau levels >41.3pg/ml 86% sensitive, 83% specific (Roerig et al 2013)
Prognostic indicators for Grade 5 dogs

- Myelography
  - Poor prognosis if contrast columns interrupted for > 5xL2 length (Duval et al, 1996)

- MRI prognostic indicators
  - CSA T2 weighted hyperintensity related to injury severity and outcome (De Risio et al, Levine et al)
  - T2 hyperintensity predictive of outcome (Ito et al)

- DTI quantification will probably be the best!
Ideal biomarker for prognosis

- Something on physical exam OR....
- Measureable in blood
- Bedside test
- High sensitivity and specificity for predicting failure to walk.
More promising biomarkers

- Remember your neurological examination
  - Muguet Chanoit et al, 2011

- Blood level of heavy chain neurofilament (pNF) – low sensitivity but high specificity
  - Nishida et al, 2014

- Blood level of GFAP to detect AMM – 75% sensitive and 98% specific
  - Sato et al, 2013
Need a combination bed side test

* Dr JiHey Lim

<table>
<thead>
<tr>
<th>In CSF</th>
<th>0</th>
<th>6h</th>
<th>12h</th>
<th>24h</th>
<th>48h</th>
<th>72h</th>
<th>96h</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-6, IL-8, MCP-1, GFAP, etc.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMP-9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CK</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MBP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glutamate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>tau protein</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>In BLOOD</th>
<th>S100β</th>
<th>NSE</th>
<th>pNF-H</th>
<th>MMP-9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time after injury</td>
<td>0</td>
<td>6h</td>
<td>12h</td>
<td>24h</td>
</tr>
</tbody>
</table>

Dr JiHey Lim
Dogs that did not regain sensation

39% (7 of 18) of these dogs did recover the ability to walk

Mean time to walking was 9m (varied from 4m to 18m)

All developed a voluntary tail wag

All were incontinent
How can we help the ones that don’t walk?

* We still don’t understand how we walk....

* Brown, 1918
Different strategies to produce recovery

• Replace neurons with the hope they will integrate with the correct networks to effect a recovery
  – Neurospheres from adult or fetal sources.
  – Embryonic neuronal transplants
Different strategies to produce recovery

• Enhance plasticity
  • Chondroitinase
  • OFG
• Rehabilitation
Different strategies to produce recovery

- Optimize function in physiologically dysfunctional but anatomically intact tissue?
Dogs recruited a minimum of 3 months after injury

- Demonstrated enhanced forelimb hindlimb coordination walking on a treadmill
- No change in measures of long tract function
- Concluded it was not a significant enough effect to warrant further investigation
Compared potassium channel antagonists with placebo in dogs that were >6 months paralyzed

- Significant improvement in open field walking, weight supported treadmill walking and owner observations
- 5 dogs had no change, 14 dogs improved with support
- 3 dogs transformed from unable to walk to walking independently.
- May help a small number of patients significantly
Potassium channel antagonists 4-aminopyridine and the t-butyl carbamate derivative of 4-aminopyridine improve hind limb function in chronically non-ambulatory dogs, a blinded, placebo-controlled trial.

--Manuscript Draft--
A recent amazing finding

Altering spinal cord excitability enables voluntary movements after chronic complete paralysis in humans

Claudia A. Angeli,1,2 V. Reggie Edgerton,3,4 Yury P. Gerasimenko3,5 and Susan J. Harkema1,2
Treatment doesn’t end with surgery

- Management of pain
- Management of incision
- Rehabilitation exercises
- Bladder care
- Mental stimulation
Any Questions?