Voor gezonde katten en honden

Stichting FelCan

FelCan Kattendag

12 maart 2016

Faculteit Diergeneeskunde, Utrecht

Universiteit Utrecht

FelCan. Organisatie: Mette Dam, e-mail: penningmeester@felcan.nl; Postbank 3035761 t.n.v. Stichting FelCan, 1154 PR Uitdam. KvK Rotterdam 24371259; website: www.felcan.nl

Voor gezonde katten en honden

Stichting FelCan

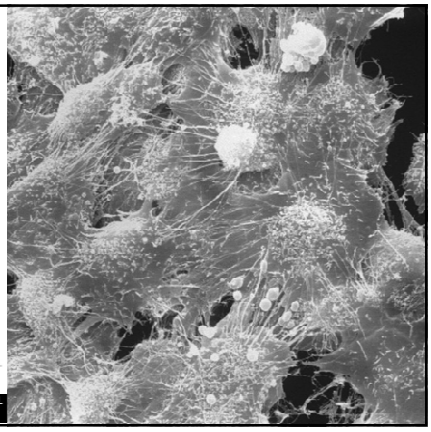
Programma

10.00	Dr. Herman Egberink, voorzitter St. FelCan. *Welkom en inleiding*
10.05-11.00	Dr. Alan Radford (lector Infectiebiologie, Universiteit Liverpool, Institute of infection and Global Health): *An update on feline calicivirus infections..*
11.00-11.50	Drs. Quirine Stassen (Dierenarts-onderzoeker, Departement Geneeskunde van Gezelschapsdieren, Faculteit Diergeneeskunde: *Epilepsie* bij de kat
11.50-12.10	***Pauze***
12.10-13.00	Dr. Chiara Valtolina (Dierenarts- specialist, Departement Geneeskunde van Gezelschapsdieren, Faculteit Diergeneeskunde: *Lipidose bij katten.*
13.00-14:00	***Lunch***
14.00-14:50	Dr. Matthijs Schilder (Onderzoeker, Departement Dier in Wetenschap en Maatschappij , Faculteit Diergeneeskunde: *Dementie-achtige verschijnselen bij de ouder wordende kat.*
14.50-15:40	Dr. Ronald Corbee (Dierenarts, specialist Klinische Voeding Gezelschapsdieren, Departement Geneeskunde van Gezelschapsdieren, Faculteit Diergeneeskunde: *Arthrose bij de kat.*
15.40	***Afsluiting van de dag***

An update on feline calicivirus infections

Dr. Alan Radford
Lector Infectiebiologie, Universiteit Liverpool, Institute of infection and Global Health

Alan Radford
alanrad@liv.ac.uk



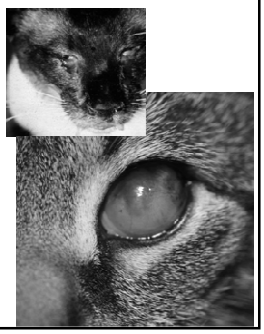
UNIVERSITY OF LIVERPOOL
THE UNIVERSITY OF LIVERPOOL
INVESTING IN KNOWLEDGE

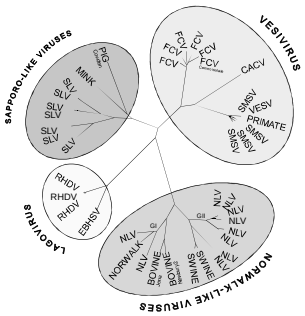
An update on feline calicivirus (FCV) infection

- Outline
  - FCV and feline herpesvirus
    - Clinical signs
    - Carrier state
  - FCV vaccination
    - Types of vaccine
    - How to evaluate vaccines
    - How to chose a vaccine

Feline viral respiratory disease

Feline Calicivirus | **Feline Herpesvirus**





Caliciviridae

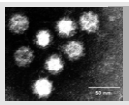
Herpesviruses

Cold sores - HSV

Infectious bovine rhinotracheitis

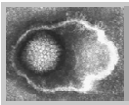
Chickenpox, shingles

Clinical disease



FCV

- oral ulceration (+ + +)
- oculonasal discharge
- conjunctivitis
- lameness

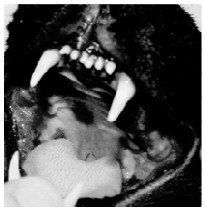


FHV

- lethargy (+ + +)
- oculonasal discharge (+ + +)
- sneezing
- salivation
- keratitis

Feline calicivirus - chronic stomatitis

- Serious condition
- Frequent euthanasia



- ASSOCIATED with FCV
- Almost 100% FCV positive
- Can't reproduce the disease

- Minimise antigenic challenge

FCV – virulent systemic disease

Kindly provided by Dr J.B. Elliott

Severe, acute systemic febrile disease

(haemorrhagic-like fever)

Often have a history of importing cats kittens with URTD

- Pyrexia
- Cutaneous oedema
- Ulcerative dermatitis
- URTD
- Anorexia
- Jaundice
- Mortality ~50%
- Adults worse than kittens
- Vaccination not protective

- FCV positive
- Individual hepatocellular necrosis
- Acute interstitial pneumonia
- Free pleural / abdominal fluid
- Intestinal crypt lesions
- Pancreatitis

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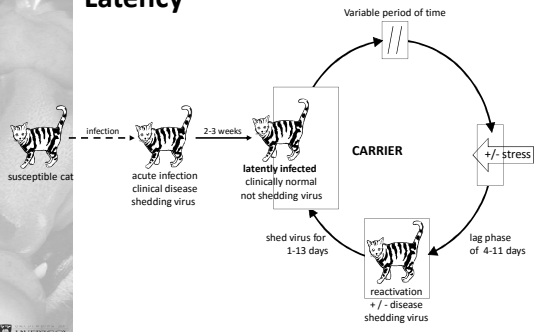
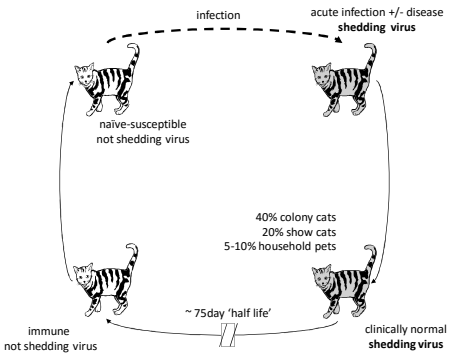
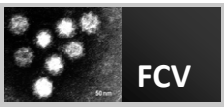
Feline herpesvirus **Latency**

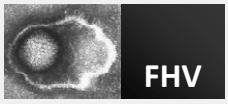


FCV - evolution



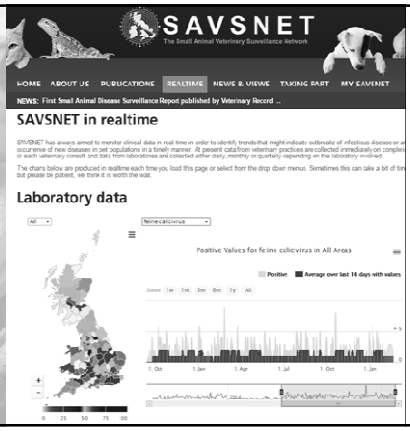
Carriers





- most (30days)
- most self cure
- evolution
- most continually shed virus
- no clinical disease

- ~100%
- life long
- latency
- intermittent reactivation
- Recrudescence



www.savsnet.co.uk

An update on feline calicivirus (FCV) infection

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    - How to chose a vaccine

VACCINATION

- Lots to be proud of!
- Vaccines marketed
  - live attenuated; subcut / im, (intranasal)
  - inactivated

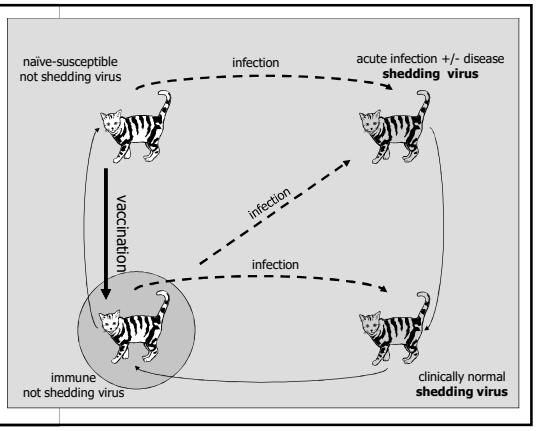
- Generally effective at preventing clinical disease
- FCV isolates in vaccines chosen to be broadly cross-reactive
  - F9 (MSD, Virbac), 255 (Zoetis), G1 and 431 (Merial)

MSD Animal Health · MERIAL · Pfizer Animal Health · Virbac Animal Health

Feline calicivirus

potential problems

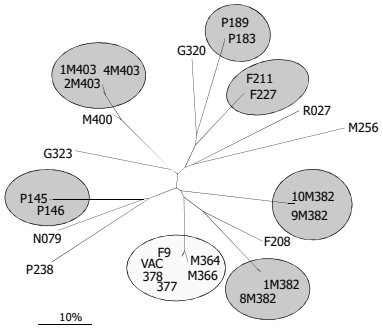
- Do not prevent infection.



Feline calicivirus

potential problems

- Do not prevent infection.
- Live vaccines may rarely cause infection (reaction).
  - if given orally
  - may generalise



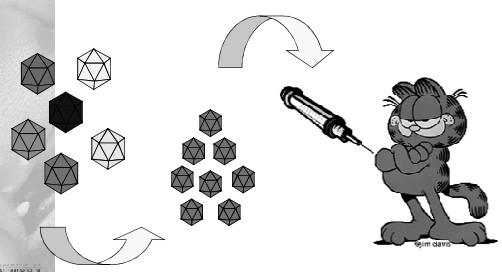
Radford et al., (2000). Veterinary Record 146, 117-123

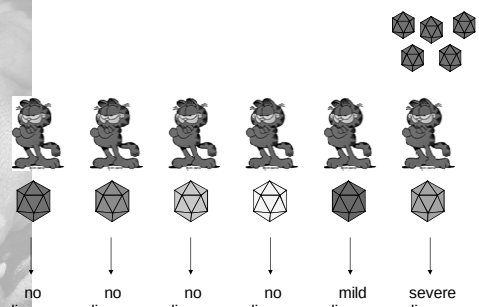
Feline calicivirus

VACCINE PROBLEMS

- Do not prevent infection.
- Live vaccines may cause infection (reaction).
  - if given orally
  - may generalise
- No vaccine will protect fully against all FCV field isolates.
  - Vaccine breakdowns.

FCV is very variable





Feline calicivirus

potential problems

- Do not prevent infection.
- Live vaccines may cause infection (reaction).
  - if given orally
  - may generalise
  - may persist
- May not protect fully against all FCV field isolates.
  - Vaccine breakdowns.
- Long term use may theoretically lead to the selection of vaccine resistant strains.

Acta Veterinaria Scandinavica

RESEARCH Open Access

Ability of vaccine strain induced antibodies to neutralize field isolates of caliciviruses from Swedish cats

Jonas Johansson Wiersma[1], Arman Sarrman[2], Anna Linche[1], Jean-Christophe Thibault[4], Louise Treiberg Berndtsson[3] and Margaret J. Hosie[2]

Conclusions: This study confirms previous observations that more recently introduced vaccine strains induce antibodies with a higher neutralizing capacity compared to vaccine strains that have been used extensively over a long period of time.

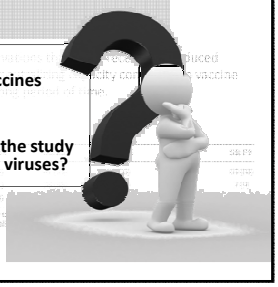
Table 1 Results of virus neutralization tests

Titres	S1; G1	S2; G1	S3; 431	S4; 431	S5; 255	S6; 255	S7; F9	S8; F9
<5	52 (67)	35 (45)	24 (31)	8 (10)	41 (53)	28 (36)	62 (79)	69 (88)
5–15	20 (26)	22 (28)	39 (50)	34 (43)	28 (36)	19 (24)	12 (15)	7 (9)
45–1215	6 (8)	21 (27)	15 (19)	36 (49)	9 (12)	31 (40)	4 (5)	2 (3)

Antisera raised against four feline calicivirus vaccine strains (G1, 431, 255 and F9) were usec in the neutrallization tests of 79 Swedish field isolates. The number of field isolates neutralized by respective antiserum s indicated, with the proportion of neutralized strains shown as a percentage within parenthesis

Things to ponder....

- **Antisera production**
  - **Is this similar to how vaccines work?**
- **Origin of isolates**
  - **Are the isolates used in the study representative of "field" viruses?**



Origin of the isolates

63 practices randomly recruited in 6 European countries:

- *UK*
- *France*
- *The Netherlands*
- *Germany*
- *Sweden*
- *Italy*

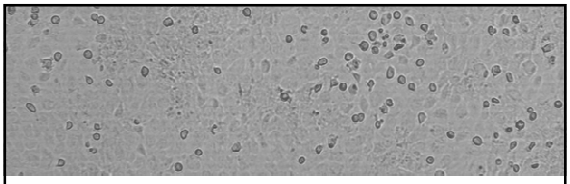
Stratified random sampling (by regions within countries) to ensure covera

LIVERPOOL

SAMPLE COLLECTION

Oropharyngeal swabs
in viral transport media

- **30 next cats (UK)**
- **40 next cats (other EU countries)**



Country	No. of practices	No. of samples	~ FCV prevalence
France	5	189	6.3%
Germany	5	176	16%
Italy	5	123	9.8%
Netherlands	3	100	16%
Sweden	5	206	8.2%
UK	27	727	8.5%

Multilevel multivariable analysis

(allowing for clustering within practice)

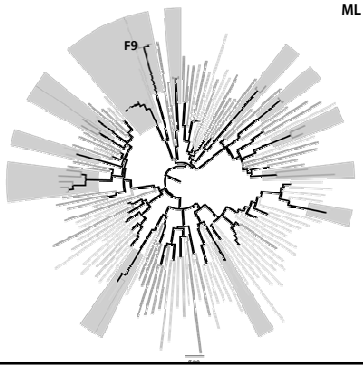
Variable		Odds ratio	95 CI% Lower	95 CI% Upper	P-value
Country					
	France	0.29	0.11	0.75	0.01
	The Netherlands		**Ref.**		
	Italy	0.234	0.087	0.631	0.004
	Germany	0.72	0.31	1.65	0.44
	Sweden	0.599	0.253	1.419	0.24
	UK	0.434	0.213	0.88	0.02
Neutered Status					
	Yes		**Ref.**		
	No	1.69	1.053	2.736	0.03
Chronic Gingivo-Stomatitis					
	Yes		**Ref.**		
	No	0.12	0.06	0.23	< 0.001
No. cats/household					
	1		**Ref.**		
	2 – 3	1.75	1.10	2.79	0.02
	4 – 10	2.82	1.49	5.31	0.001
	> 11	0.74	0.08	6.97	0.79
Age (month)		0.99	0.99	0.99	0.01

~ Porter et al, 2005, Helps et al 2005, Binns et al 2000

~ Coyne et al, 2012; Porter et al, 2005

PHYLOGENETIC ANALYSIS (country)

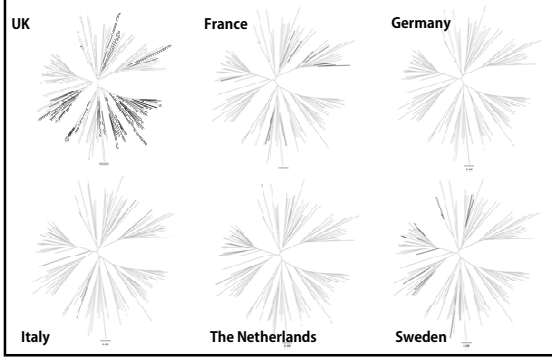
ML capsid tree, GTR+G+I



- 109 strains on capsid tree
- no predominant strain
- field strains restricted to 1 country
- largest cluster of 7 vaccine like isolates
- no evidence for widespread or international transmission

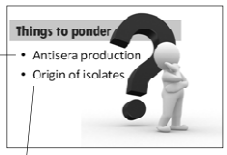
France
Germany
Italy
Netherlands
Sweden
United Kingdom

PHYLOGENETIC ANALYSIS (country)



Neutralisation tests.

Cats vaccinated with 10x dose Nobivac Tricat at 9 and 12 weeks



Cross sectional random collection in practice

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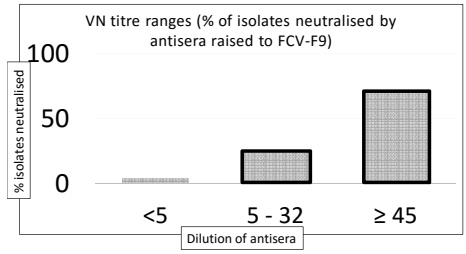
RESULTS



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How do you choose a vaccine?

How do you choose a vaccine?

- The cheapest one?
- The one the owner wants?
- (Parenteral or topical)?
- Type of FCV?
- Live or inactivated?
- Manufacturer?

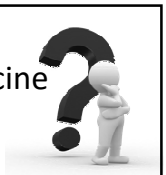
How do you choose which one?

- The cheapest one?
- The one the owner wants?
- (Parenteral or topical)?
- **Type of FCV?**
- **Live or inactivated?**
- Manufacturer?

Live vs Killed

Live	Killed
• Virus is weakened (attenuated) so it is less likely to cause disease	• Virus is 'killed'
• Virus is still 'live'	• No chance of causing infection or disease
• Limited replication stimulates immune response	• Often need adjuvants to stimulate immune response
• May under rare conditions cause infection and mild disease.	• Adjuvants have greater association with sarcomas
• Not licensed during pregnancy	• Licensed during pregnancy

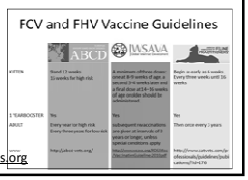
How to choose a vaccine



- If it isn't broken, don't fix it
- Inactivated in closed colonies, pregnant queens, immunosuppressed
- FCV antigen choice. Consider a different antigen if you are getting disease despite regular vaccination
- Consider what you need to vaccinate against

Summary?

- FCV remains common in the cat population
- Even healthy cats can shed the virus
- Wide range of signs
- Vaccinations good at reducing clinical disease
- Companies may try to achieve market advantage based on strain
- Find out what type of vaccine you use



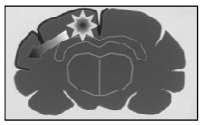
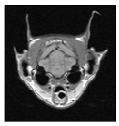
www.abcdcatsvets.org

Epilepsie bij de kat

Drs. Quirine Stassen
Dierenarts-onderzoeker, Departement Geneeskunde van Gezelschapsdieren,
Faculteit Diergeneeskunde:

EPILEPSIE BIJ DE KAT
Vallen, opstaan en weer doorgaan?

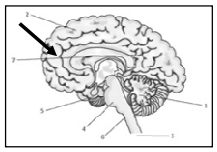
FelCan Kattendag – 2016
Quirine Stassen

Epileptische aanval

Aanvalsgewijs optreden van motorische, autonome of gedragsmatige verschijnselen

t.g.v. abnormale synchrone / overmatige neuronale activiteit in cerebrum



Epilepsie

Het herhaald optreden van epileptische aanvallen

Ddx Paroxysmale aandoeningen kat

- Epilepsie
- Flauwte
  - t.g.v. hypoxie hersenen
- Gedragsprobleem
- Pijn
- Feline hyperesthesia syndrome
- (Feline vestibular syndrome)
- Narcolepsie / kataplexie
- Myoclonus
- Paroxysmale dyskinesie

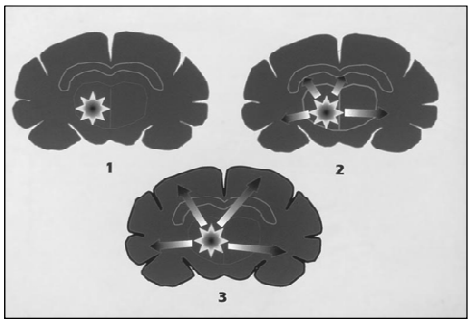
INDELING TOEVALLEN

- Semiologie
- Oorzaak

Semiologie

- Gegeneraliseerd
- Focaal
- Focaal overgaand in gegeneraliseerd

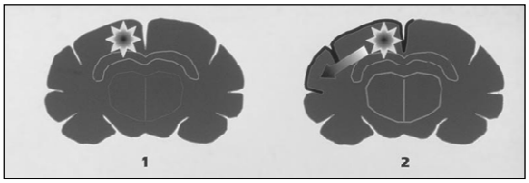
Gegeneraliseerde toeval



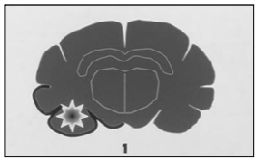
Gegeneraliseerde toeval

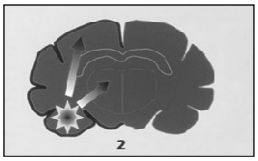
- Prodroom
- Ictus (inclusief aura)
- Post-ictale fase

Focale toeval

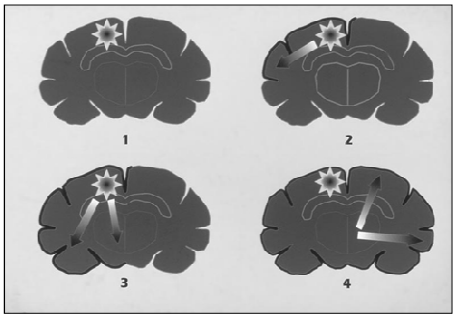


Atypische focale toeval





Focaal overgaand in gegeneraliseerd



CLUSTERING

Meerdere toevallen in korte tijd met pre-ictale fase, ictus en post-ictale fase

Status epilepticus

Continue epileptische activiteit > 5 min /

Meerdere aanvallen achter elkaar zonder volledig herstel CZS functies tussendoor

Oorzaken epilepsie

- Idiopatische epilepsie (primair) 21-59 %
  - oorzaak onbekend
- Structurele epilepsie (secundair) 47-50%
  - oorzaak in grote hersenen
- Reactieve epilepsie 22 - 31%
  - stofwisselingsziektes / vergiftiging

Clinical characterization of epilepsy of unknown cause in cats. Wahle et al. 2014
Etiologic classification of seizures, signalment, clinical signs and outcome of cats with seizure disorders. Schriefl et al. 2008

Idiopatische epilepsie

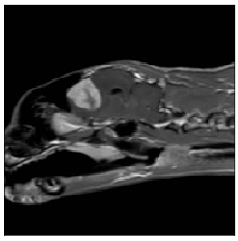
- 1e Aanval jonge leeftijd (gem. 3.5 jaar)
- Meestal gegeneraliseerde epilepsie
- Geen andere symptomen
- Lichamelijk onderzoek: g.b.
- Bloedonderzoek: g.b.
- MRI hersenen g.b.

Reactieve epilepsie

- Hepatoencephalopathie
- Uremische encephalopathie
- Hypoglycemie
- Hypocalcemie
- Hypo / hypernatriemie
- Thiamine deficiëntie
- Hyperthyreoidie?

Structurele epilepsie - Vitamin D -

- Vasculair
- Inflammatoir
- Trauma
- Toxinen
- Anomalie
- Metabool
- Idiopatisch
- Neoplasie
- Degeneratief



Structurele epilepsie

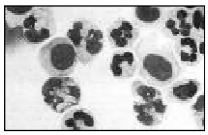
Vasculair	Hypertensie Ischemische encephalopathie Thromboembolie Polycytemie
Inflammatoir: •Infectieus	 Toxoplasma FIP FeLV FIV Bartonella Parasieten migratie Cryptococcen Bacterieel
•Immuungemedieerd	Niet suppuratieve ME
Toxinen	Organophosfaten Lood Ethyleenglycol

Structurele epilepsie

Trauma	
Anomalie o.a.	Hydrocephalus
Metabool	Reactieve epilepsie
Neoplasie • Primair o.a. • Metastasen	 Meningioom Maligne lymfoom Glioom Hypofyse adenoom/adenocarcinoom Choroid plexus tumor Adenocarcinoom vanuit de neus
Degeneratief	Stapelingsziekte

Diagnostisch plan

- Signalement en anamnese
- Lichamelijk onderzoek
- Bloedonderzoek
  - NH3 (galzuren)
  - Glucose
  - Na, K, Ca
  - Kreatinine / ureum
  - Ht, leuco's en diff.
- Bloeddrukmeting (kat)
- MRI / CT
- Onderzoek CSF
- (EEG)



Therapie

- Oorzaak bestrijden
- Anti-epileptica (AE)

Antiepileptica

- Wanneer beginnen
- Juiste keuze AE en juiste dosering
- Monitoren
- Wanneer dosering aanpassen
- Wanneer wisselen van AE / nieuw AE toevoegen
- Motiveren eigenaar

Therapie; wanneer starten met AE?

- > 1 toeval per 6 weken (IVETF: 6 mnd!)
- Langdurige ictus
- Cluster aanvallen
- Status epilepticus
- Ernstige / langdurige post-ictale verschijnselen
- Progressief verloop: toename frequentie, duur, ernst
- Eerste toeval na ernstig hoofdtrauma
- Structurele hersenlaesies op MRI / CT

Therapie; voorlichting eigenaar

- Veel patiënten blijven toevallen houden
- Niet curatief!
- Levenslang. **Niet plotseling stoppen!**
- Herhaald aanpassen dosering nodig
- Geef medicatie de kans!
- Risico clusters, SE
- Bijwerkingen

Anti-epileptica kat

- Fenobarbital
- Levetiracetam (Keppra®)
- Diazepam (Valium®): liever niet
- Clonazepam: liever niet
- Zonisamide: ?
- Gabapentine: ?
- Pregabalin: ?
- Imepitoine (Pexion®): ?
- Kaliumbromide (Epikal®): NEE!
- Fenytoine (Epitard®): NEE!

Fenobarbital (Phenoral®)

- Oraal, iv, im
- Indicatie: 1e keus onderhoudstherapie
- Monotherapie / combi
- Effectief
- Relatief veilig, bijwerkingen m.n.: ataxie, sedatie, pu/pd, pf, beenmerg hypoplasie, overgevoeligheid
- T ½: 34-50 uur → SS: 10 dagen
- **Start**dosis:
  oraal 1,5 – 2 mg/kg 1 - 2 dd

Levetiracetam (Keppra®)

- Oraal / s.c./ i.m. / i.v.
- Indicatie:
  - add on onderhoudstherapie
  - noodmedicatie
- Effectiviteit?
- T ½: 3 uur → frequent doseren
- Weinig / milde bijwerkingen: sedatie. anorexie
- **Start**dosering:
  - onderhoud: 20 mg/kg 3dd oraal

Diazepam

- Oraal / im / iv / rectaal
- Niet combineren met FB of andere BZD
- Indicatie:
  - couperen toeval / status epilepticus
  - onderhoudstherapie
- Relatief effectief
- Bijwerkingen: sedatie, risico fulminante hepatitis , pf,
- Onderhoud: 0,5 - 2 mg/kg **over** 2 - 3 dd
  Spoedeisend: 1 mg/kg i.v. of 2 mg/kg rectaal
- Monitoring leverwaarden (ALAT, ASAT)

Advies: liever niet als onderhoudstherapie

Clonazepam

- Oraal
- Indicatie: onderhoudstherapie
- Niet combineren met FB of andere BDZ
- Indicatie: onderhoudstherapie
- Bijwerkingen: sedatie, ataxie, fulminante hepatitis?
- Onderhoudsdosering: 0,5 mg per kat, 1 tot 2 dd
- Monitoring leverwaarden

Advies: liever niet!

Kaliumbromide

- Matig effectief in katten
- Bijwerkingen: groot risico ernstige allergische bronchitits (53-42%), sedatie, ataxie, pu/pd, polyfagie, braken, NB: niet hepatotoxisch
- T½: 11 dagen → SS 2 maanden!

Advies niet gebruiken bij de kat!

Gabapentine

- Oraal
- Indicatie: onderhoudstherapie
- Monotherapie / add on
- Effectiviteit?
- Bijwerkingen: sedatie, ataxie
- Onderhoudsdosering:
- - Start: 5-10 mg/kg 1 dd,
- - Daarna: 5-10 mg 2 dd

Andere anti-epileptica

- Pregabalin
- Zonisamide
- Imepitoine

Nog onvoldoende bewijs effectiviteit / kennis farmacokinetiek / bijwerkingen

Treatment failure

< 50% reductie in aanvalsfrequentie

- Progressieve aandoening
- Dosering te laag
- Onvoldoende therapietrouw
- Therapieresistente voor gebruikte AE

↓

Aanpassen therapie

Aanpassing dosering AE (1)

- Geef medicatie de kans!
  - Fenobarbital: 2 wk
  - Levetiracetam: 2 d
- Onvoldoende effect / bijwerkingen → bloedspiegel
  - Fenobarbital:
    - Therapeutische spiegel: 10-40 µg/ml
    - "Ideale" spiegel: 25-30 µg/ml
  - Levetiracetam
    - Therapeutische spiegel 5-45 µg/ml ???

Aanpassing dosering / AE (2)

- Indicatie: onvoldoende effect nadat steady state is bereikt.
  *Fenobarbital:
  - 25-50%↑ of
  - (gewenste spiegel / huidige spiegel) x huidige dosering = nieuwe dosering

  *Levetiracetam
  - Verhoog met stappen van 10-20 mg/kg op effect.

Toevoegen AE

- Indicatie
  - onvoldoende effect i.c.m. maximale bloedspiegel / dosering
  - onacceptabele bijwerkingen
- Voorbeeld
  *FB + levetiracetam
  - verlaag FB met 25% indien effectieve controle en bijwerkingen

Stoppen AE

Indicatie

•> 1 jaar toevalsvrij

- geleidelijk afbouwen over periode van maanden

• Levensbedreigende bijwerkingen

- opname
- stoppen 1e AE
- loaden 2e keus AE

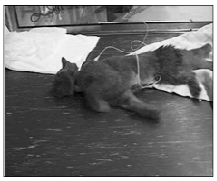
Alternatieve therapieën

- Vagal nerve stimulation
- Dieet
- - Ketogeen dieet
- - Hypoallergeen dieet

Status epilepticus

Spoed!!

- Hyperthermie
- Hypoxie
- Hypotensie
- Nierfalen
- DIS
- Verslikpneumonie
- Hartfalen



Status epilepticus 1

SPOED!!!

1. **Diazepam**
- Iv (start 0,5 – 1 mg/kg)
- Eventueel rectaal (1 - 2 mg/kg)
- Bij onvoldoende effect:
- herhalen (i.v. na 2 min, rectaal na 10 min, maximaal 3x) of
- CRI 0,5-2 mg/kg/uur
- Monitor P, A, T, bloeddruk
- Langer dan 24 uur toevalvrij → geleidelijk afbouwen

Status epilepticus 2

2. Indien onvoldoende effect:

Fenobarbital

- langzaam iv 2 - 6 mg/kg, max effect na 30 min) of
- i.m.. 2 x met 10 min er tussen
- daarna
  - CRI: 2-4 mg/kg/uur of
  - IM: 6 mg/kg iedere 6 uur (of o.g.v. bloedspiegel)

3. Indien onvoldoende effect:

Propofol toevoegen

- langzaam iv op effect, 1-6 mg/kg
- Daarna: CRI: 6-15 mg/kg/uur

Status epilepticus 3

Alternatief indien sedatie gecontra-indiceerd is:

- Levetiracetam
  - Bolus 20 mg/kg
    ↓
- Onderhoud met levetiracetam / fenobarbital

Status epilepticus 4
- Monitoring -

4. Monitor A, P, T, bloeddruk
5. Cave hyperthermie
6. Vloeistoftherapie
7. Intubeer en ventileer indien nodig
7. Bloedonderzoek: glucose, Ca, (Na, K)

Status epilepticus 5

Indien:
- Hypertherm
- Verdacht hersenoedeem
- Toeval > 15 min.

↓

- Koelen i.g.v. T > 41,0 ^{o}C
- Mannitol (1,0 g/kg i.v. over 15 min.)
- Thiamine (2 mg/kg i.m.)

Lipidose bij katten

Dr. Chiara Valtolina
Dierenarts- specialist, Departement Geneeskunde van Gezelschapsdieren,
Faculteit Diergeneeskunde:

A clinical approach to feline hepatic lipidosis(FHL)

Chiara Valtolina DVM, Dipl. ACVECC , Dipl ECVECC
Intensive Care Unit, Faculty of Veterinary Medicine Utrecht,
The Netherlands

Introduction

- Lizzy
- Clinical features of FHL
- Clinical conditions related to FHL
- Pathophysiology
- Diagnostic protocol
- Treatment

Lizzy

- 4 years old female neutered Siberian cat
- Anamnesis:
  - Lethargy and intermittent vomiting for a couple of week
  - Dysorexia for a week
  - Anorexia since 5 days

Lizzy

- Physical examination
  - Lethargic but responsive
  - Cardiorespiratory unremarkable
  - Marked icterus sclera, skin and mucous membrane
  - 7 % dehydrated
  - Haepatomegaly
  - Body condition score 4/9

Lizzy

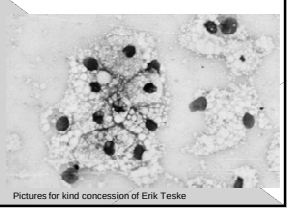
- Problem list
  - Lethargy
  - Dehydration
  - Icterus
  - Haepatomegaly
  - Vomiting
  - Anorexia

Lizzy

- Clinicopathologic findings
  - Ht 0.35 (35-45)
  - Inflammatory leucogram
  - Tp 69 g/L (54-70)
  - Albumin 20 g/L (20-26)
  - ALT 260 U/L (30-73)
  - Bile acid 85 µmol/L (<13)
  - Potassium: 2.7 mmol/l (3.6-4.6)
  - Glucose: 7.4 mmol/L (4.2-5.5)
  - Coagulation profile: mildly abnormal

Lizzy

- Abdominal ultrasound:
  - Enlarged and hyperechoic liver
  - Hypoechoic pancreas and hyperechoic fat surrounding
- Liver citology
  - Hepatic lipidosis



Pictures for kind concession of Erik Teske

Hepatic lipidosis

- First description in 1977
- Most common hepatobiliary disease in cats
- Prevalence of 0.16% in a population cats at primary care practices

- Middle- aged adult cats
- No breed or sex predilection
- Most cats are "over-conditioned" at presentation

Feline Hepatic Lipidosis

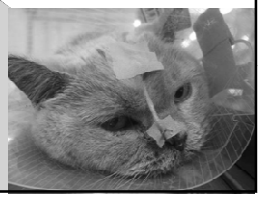
Anorexia and "stress"

- "Primary lipidosis"
  - Temporary decreased food intake
  - Change in food palatability
  - Period of forced weight loss
  - Stressful situation

Feline Hepatic Lipidosis

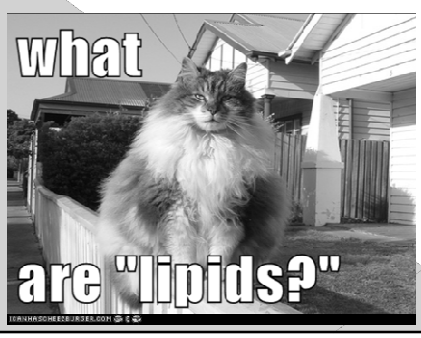
Anorexia and "stress"

- "Secondary lipidosis "
  - Other hepatic disease
  - Small intestinal disease
  - Pancreatitis
  - Neoplasia
  - Diabetes mellitus
  - Chronic kidney disease

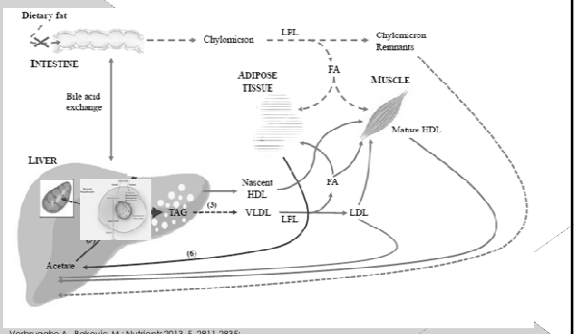


Pathophysiology

Pathophysiology of feline hepatic lipidosis



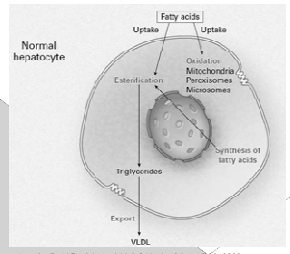
Lipid metabolism in the cats



Verbrugghe A., Bakovic, M.; Nutrients 2013, 5, 2811-2835;

Lipid metabolism in the cat

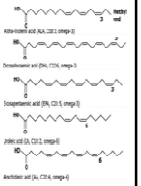
- FFAs within the liver
  - Some used as energy(oxidized)
  - Some esterified in triglyceride
  - Some make phospholipids and cholesterol

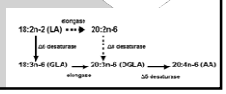


Angulo, P.; N Engl J Med, Vol. 346, No. 16, April 18, 2002

Fatty acid metabolism in cats: Essential Fatty Acid (EFA)

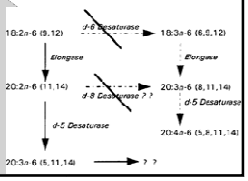
- Linoleic acid(n-6) and a-linoleic acid(n-3) are considered EFA for all mammals
- Other mammals <u>can</u> synthesise via elongase and Δ saturase the long chain poly-unsaturated fatty acid (LC-PUFA):
  - arachidonic acid (AA n-6)
  - docosahexanoic acid (DHA n-3)
  - eicosapentanoic acid (EPA n-3)





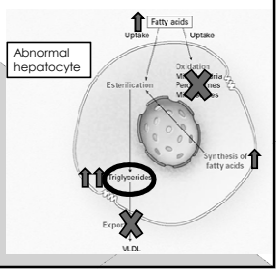
Fatty acid metabolism in cats: Essential Fatty Acid (EFA)

- Cats and other obligated carnivores are unable to synthesise sufficient the LC-PUFAs AA, DHA and EPA from linoleic and a-linoleic acid
- Limited Δ 5 and Δ 6 desaturases



Pathophysiology of FHL

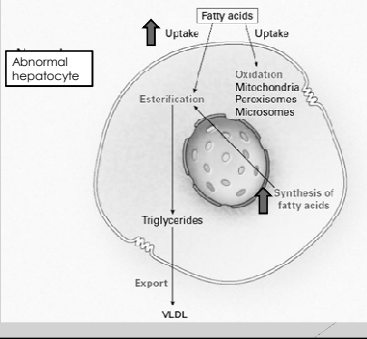
- Characterised by the accumulation of triglycerides (TGs) in the hepatocytes
- Imbalance between:
  - Peripheral fat stores mobilized to the liver
  - *De novo* lipid synthesis
  - Hepatic use of fatty acids (FAs) for energy
  - Hepatic dispersal of triglycerides



Pathophysiology of FHL

- Secondary to:
  - Cat unique lipid metabolism
  - Cat unique amino acid and protein metabolism
- Predisposing factors:
  - Obesity and insulin resistance
  - Protein and amino acid and B-vitamin deficiency
  - L-carnitine deficiency
  - Reduction of antioxidant availability
  - Essential fatty acid deficiency

Increased FAs accumulation in the liver



Increased FAs accumulation
Where are FAs coming from?

Lipid Composition of Hepatic and Adipose Tissues From Normal Cats and From Cats With Idiopathic Hepatic Lipidosis

Jean A. Hall, Louise A. Barstad, and William E. Connor

The purpose of this study was to characterize the lipid classes in hepatic and adipose tissues from cats with idiopathic hepatic lipidosis (IHL). Concentrations of triglyceride, phospholipid phosphorus, and free and total cholesterol were determined in lipid extracts of liver homogenates from 5 cats with IHL and 5 healthy control cats. Total fatty acid composition of liver and adipose tissue was also compared. Triglyceride accounted for 34% of liver by weight in cats with IHL (338 ± 38 mg/g wet liver) versus 1% in control cats (9.9 ± 1.0 mg/g wet liver, $P < .001$). The mass of cholesterol ester was significantly higher in triglyceride-free (TG-free) liver from cats with IHL (741 ± 340 μg/g TG-free wet liver) compared to healthy cats (31 ± 11 μg/g TG-free wet liver, $P < .05$). Total fatty acid composition of hepatic tissue in the 2 groups differed; palmitate was higher (19.5 ± 1.1% of total fatty acids in cats with IHL versus 9.2 ± 2.7% in controls, $P < .05$), stearate was lower (8.5 ± 0.3% versus 16.8 ± 1.1%, $P < .05$), oleate was higher (41.2 ± 1.5% versus 31.1 ± 1.8%, $P < .05$), and arachidonate was lower (1.2 ± 0.2% versus 6.0 ± 0.9%, $P < .05$). The total fatty acid composition of adipose tissue also differed between the 2 groups; palmitate was higher (25.2 ± 1.2% in cats with IHL versus 21.3 ± 0.6% in controls, $P < .05$), total monounsaturated fatty acids were higher (48.4 ± 1.0% versus 45.0 ± 0.8%, $P < .05$), linoleate was lower (13.3 ± 1.6% versus 17.5 ± 0.9%, $P < .05$), total (n-6) fatty acids were lower (13.8 ± 1.36% versus 18.4 ± 0.83%, $P < .05$), linolenate was lower (0.2 ± 0.04% versus 0.7 ± 0.06%, $P < .05$), and total (n-3) fatty acids were lower (0.3 ± 0.02% versus 1.3 ± 0.32%, $P < .05$). The fatty acid composition of both liver and adipose tissue was similar for stearate, oleate, linoleate, and linolenate in cats with IHL. These results support the hypothesis that the origin of hepatic triglyceride in cats with IHL is the mobilization of fatty acids from adipose tissue.

J Vet Intern Med 1997;11:238–242. *Copyright © 1997 by the American College of Veterinary Internal Medicine.*

Increased FAs accumulation
Where are FAs coming from?

- Increased level of palmitate (16:0) in visceral adipose tissue (VAT) and liver of lipidotic cats
- FAs mobilisation occurs from VAT and omental fat tissue
- This is also one of the reason why obese cats , who have an increased deposition of VAT compared to lean subject are more predispose to lipidosis

Increased FAs release from peripheral store

J Vet Intern Med 2000;14:26–36

Metabolic and Hormonal Alterations in Cats with Hepatic Lipidosis

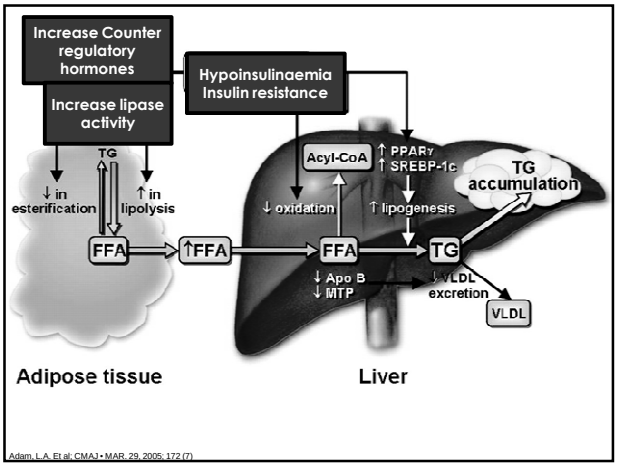
Bonnie Brown, Glenna E. Mauldin, Joel Armstrong, Scott D. Moroff, and G. Neal Mauldin

Hepatic lipidosis in cats is a commonly diagnosed hepatobiliary disease of unknown cause. The purpose of this prospective study was to characterize the blood hormone and lipid status of cats with hepatic lipidosis, and to compare this status to that of cats with other types of liver disease and to control cats. Twenty-three cats with hepatic disease were assigned to 1 of 2 groups on the basis of cytopathologic or histopathologic examination of the liver: group 1, hepatic lipidosis (n = 18); or group 2, cholangiohepatitis (n = 5). Ten healthy young adult cats were used as controls. Food was withheld from control animals for 24 hours before blood collection. Concentrations of plasma glucagon and serum insulin, cortisol, thyroxine, triglycerides, cholesterol, phospholipids, and nonesterified fatty acids (NEFAs) were determined in all cats, in addition to routine hematologic and serum biochemical testing. Cats with hepatic lipidosis had higher serum NEFA concentrations than cats with cholangiohepatitis or control cats ($P < .05$). Cats with cholangiohepatitis had higher serum cholesterol and phospholipid concentrations than those of cats with lipidosis or control cats ($P < .05$); their plasma glucagon concentrations were higher than those of control cats ($P < .05$), but were not different from those of cats with hepatic lipidosis. Serum insulin concentrations were significantly higher in control cats than in diseased cats ($P < .05$), but neither serum insulin nor the insulin to glucagon ratio was significantly different among the cats with hepatic disease. The high concentration of NEFAs in cats with hepatic lipidosis suggests that at least 1 factor in the pathogenesis of this syndrome may involve the regulation of hormone-sensitive lipase.

Key words: Anorexia; Cholangiohepatitis; Glucagon; Insulin; Nonesterified fatty acid; Triglyceride.

Increased FAs release from peripheral store

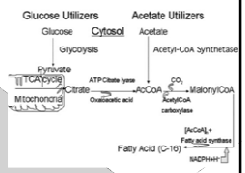
- Metabolic changes in lipidosis:
  - Decrease serum insulin level
  - Decrease in insulin: glucagon ratio



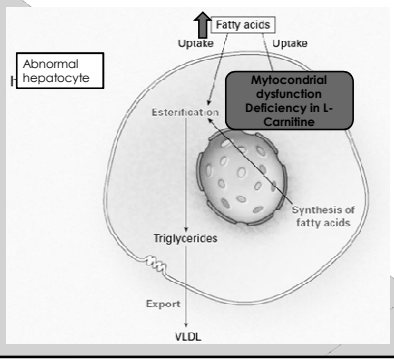
Adam, L.A. Et al; CMAJ • MAR. 29, 2005; 172 (7)

Where are FAs in FHL coming from?
De novo lipogenesis (DNL) of FAs

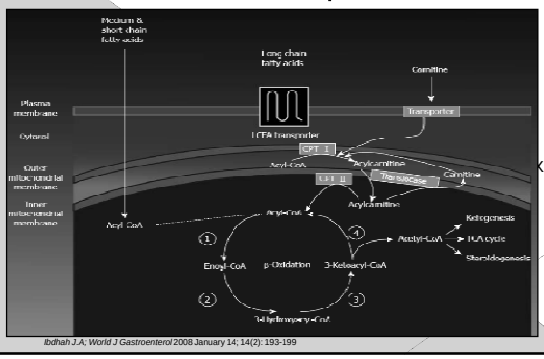
- Substrate for DNL is in the strict carnivores acetate and not glucose
- Site for DNL is adipose tissue then liver, mammary gland and muscle
- Palmitate (16 : 0) is the end product
- In FHL palmitate is increased in adipose tissue and liver



Limited oxidation of FFA



Limited oxidation of FAs
Mitochondrial dysfunction



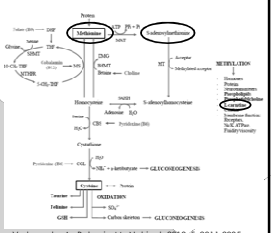
Ibdhah J.A; World J Gastroenterol 2008 January 14; 14(2): 193-199

Limited oxidation of FAs
Mitochondrial dysfunction

- The mitochondrial abnormalities associated with NAFLD:
  - Ultrastructural lesions
  - Depletion of mitochondrial DNA
  - Decreased activity of respiratory chain complex
  - Impaired mitochondrial β-oxidation
- Center et al. reported mitochondrial abnormalities in FHL

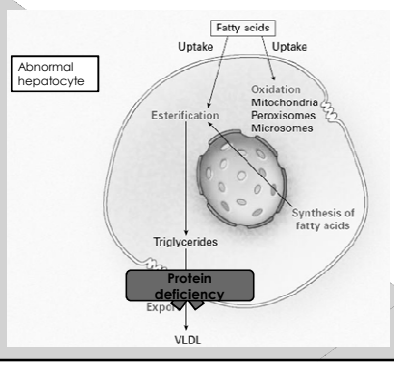
Limited oxidation of FAs
L-carnitine deficiency

- Carnitine synthesis occurs mainly in the liver
- Methionine and S-adenosyl-methionine (SAMe) important for carnitine synthesis
- In FHL methionine deficiency reported



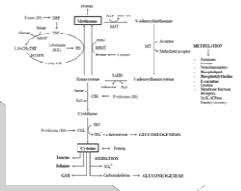
Verbrugghe A., Bakovic, M.; Nutrients 2013, 5, 2811-2835;

Inappropriate secretion of VLDL



Inappropriate secretion of VLDL Proteins deficiency

- Cats possess limited ability to adjust protein metabolic pathways to conserve nitrogen
- Plasma concentrations of alanine, citrulline, arginine, taurine and methionine >50% reduced in FHL



Verbrugghe A., Bakovic, M.; Nutrients 2013, 5, 2811-2835;

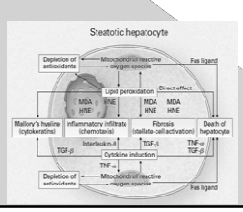
- Decrease in Apolipoprotein B100

Inappropriate secretion of VLDL Proteins deficiency

- Cats with FHL show:
  - Increased serum TG
  - Increased VLDL plasmatic concentration
  - Increased LDL enriched with TG
  - Hyperlipidaemia
- VLDL secretion seems increased…. but possibly not enough to keep up with TG accumulation in liver

Accumulation of trygliceride

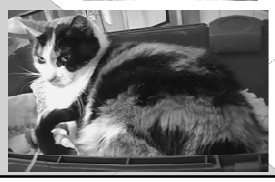
- Distension of hepatocites with TG
- Reduction of number and function of organelles
- Abnormla function of hepatocytes mitochondria
- Production of reactive oxygen species and of cytokines



FLH

Clinical signs

- Jaundice, vomiting, dehydration
- Ptyalism
- Poor hair coat
- Hepatomegaly



Clinical signs

- If hepatic encephalopathy:
  - Depression, stupor

FLH

Clinicopathologic findings

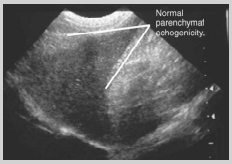
- ⇧⇧ T Bilirubin, ALP
- Increased AST, ALT, bile acids
- Altered coagulation profile
- Hyperglicaemia, hypokalaemia, hypophosphatemia

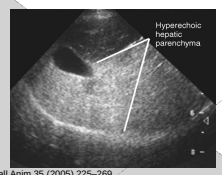
- Ammonia can be elevated in case of hepatic encephalopathy

FLH

Diagnosis

- Anamnesis
- Clinical signs
- Clinicopathologic findings
- Abdominal ultrasound



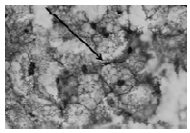


Picture taken from : S.A. Center "Feline hepatic lipidosis" Vet Clin Small Anim 35 (2005) 225–269

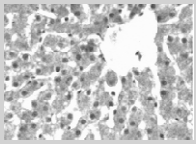
FLH

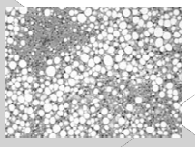
Diagnosis

- Fine needle aspiration of the liver



- Liver biopsies (?)





Pictures taken from: P.J.Armstrong and G Blanchard "Hepatic lipidosis in cats". Vet Clin Small Anim 39 (2009) 599–616

Treatment in cats

- Fluid therapy and electrolytes correction
  - Isotonic crystalloid (LRs, NaCl 0.9%)
- Maintenance
  - 40-50 ml/kg/day
- Supplementation
  - Hydration deficit:
    % dehydration x 10 x BW (kg)

FLH

Treatment in cats

- Supplementation
  - Potassium supplementation:
    $(4.5 - [K^+])x\ 0.6 \times BW = ?$ mmol)
    rate: < 0.5 mmol/kg/h
  - Phosphate supplementation
    0.03-0.12 mg/kg IV for 6 hours

FLH

Treatment in cats

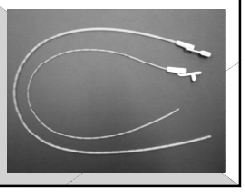
EARLY NUTRITIONAL SUPPORT!!!

Enteral nutrition

Enteral nutrition

The use of feeding tubes

- Naso-oesophageal feeding tube
  - Tube (3.5-5 Fr) from the nose to caudal oesophagus
  - Easy to place without general anaesthesia
  - Temporary solution
  - Only liquid diets (Convalescence Royal Canine)



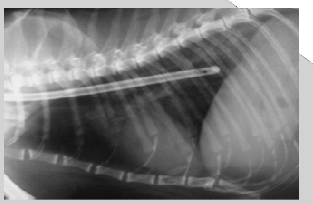
The use of feeding tubes

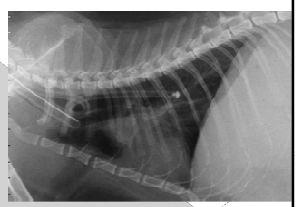
- Oesophageal feeding tube
  - Tube (12-14 French)
  - Require brief general anaesthesia and experience to be positioned
  - Well tolerated and long term solution
  - Liquid or soft diets (convalescence Royal Canine A/d Hill's ,Recovery support Eukanuba..)

Enteral nutrition
Naso-oesophageal feeding tube

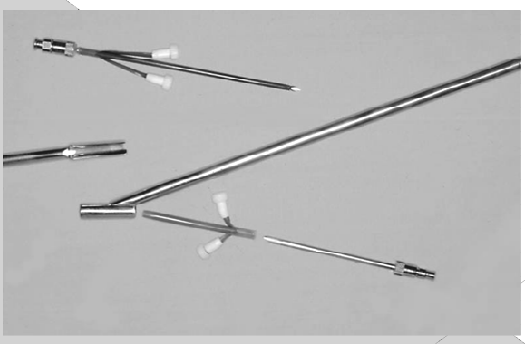
Enteral nutrition
Oesophageal feeding tube

Oesophageal feeding tube



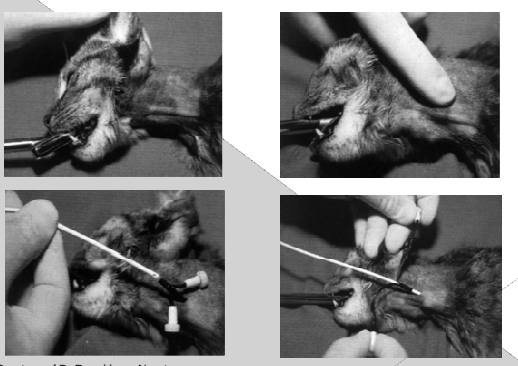


Oesophageal feeding tube



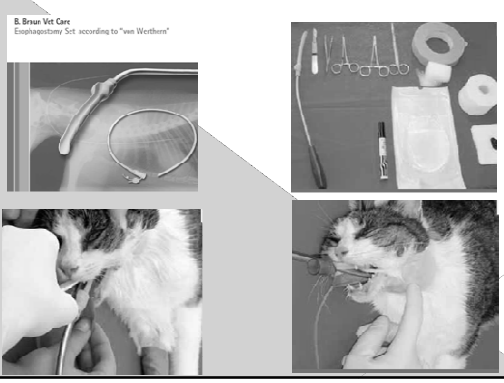
Courtesy of Dr Ronald van Noort

Oesophageal feeding tube

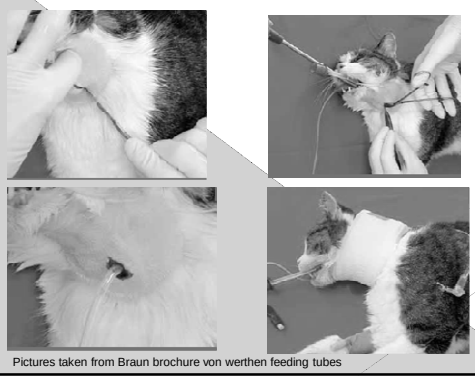


Courtesy of Dr Ronald van Noort

Oesophageal feeding tube



Oesophageal feeding tube



Pictures taken from Braun brochure von werthen feeding tubes

How much to administer

- Calculate the resting energy requirement (RER) that the animals needs based on its weight
- RER (resting energy requirement)
  - Amount of calories that an animal in a neutro thermal environment requires per day

How much to administer

- Nutritional reccomendation
  - RER : 50 -60 Kcal/kg BW/d

  - Administration diet rich in protein (30%–40% of RER), moderate in lipids (about 40% RER), and relatively poor in carbohydrate (about 20% of RER)

Enteral nutrition
Feeding program

- Once obtained the RER , calculated how many ml of food the cat requires per day
- Day 1
  - Administer 1/3-1/2 of the energetic requirement
  - Monitor response cat to feeding and electrolytes
- Day 2
  - Full amount necessary

Enteral nutrition
Re-feeding syndrome

- Syndrome associated with caloric repletion of the starved patient
  - Insulin release
  - Cellular uptake of phosphorus and potassium
- Clinical findings:
  - Hypophosphataemia, hypokaliemia, anaemia
  - Lethargy, vomiting , diarrhoea, tachypnoea

Which diet to use

- Liquid :
  - Fortol C
  - Enteral care
  - Convalescence (Royal Canine)
- Soft :
  - a/d Hill's
  - High calory Eukanuba
  - Recovery Royal Canine
- Specific diet blenderised

Enteral nutrition

- Depending on the cat ability to tolerate food
  - Daily amount (in ml) divided in 4-6 meals
  - Food administered via continuous rate infusion (CRI)

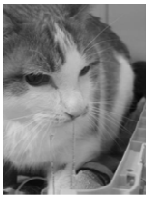
Monitoring

- Re-evaluate nutritional requirement
- Monitoring body weight
- Daily check of catheter for inflammation , discharge pain
- Monitor electrolytes

When do I stop nutritional support ?

- Cat that :
  - Eats normally for one/two days
  - Able to maintain his/her body weight
- Improvement of the underlying disease

Treatment in cats



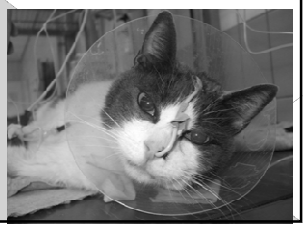
Antiemetic and antinausea

- Metoclopramide
  1mg/kg/day CRI
  0.2-0.5 mg/kg q8h SC, IV
- Maropitant
  0.5mg/kg sc once a day
- Ondansetron
  0.25-0.5 mg/kg q8-12 h IV, SC

Treatment in cats

Antiemetic and antinausea

- Ranitidine
  2mg/kg IV slowly q12 h
- Omeprazol
  1 mg/kg q12 h IV



Treatment in cats

- Cobalamine (vit B12) supplementation
- Vit K supplementation
  - 0.5-1.5 mg/kg SC q 8 h
- N-acethylcysteine
  - 140 mg/kg (20% solution diluted 1:4 or greater with saline) then 70mg/kg every 8 h
- S-adenosylmethionine (SAMe)
  - 18 mg/kg

Treatment in cats

- Ursodeoxycolic acid
  - 10 to 15 mg/kg PO once a day
- L-carnitine and taurine supplementation
  - 250 mg of each, q 12 -24 h

FLH

Prognosis

- Depends on:
  - Underlying disease
  - Timing of starting nutritional support
- Good prognostic factors: younger age and higher normal serum potassium concentration and normal hematocrit
- Bilirubin decrease of 50% in 7-10 days if resolution of disease

Hepatic lipidosis

- Common hepatobiliar disease in cats
- Anorexia, stress are predisposing factor
- Pathophysiology incompletely understood
- Diagnosis is based on anamnesis, clinical signs and echographic and cytological confirmation
- Early nutritional support is the most important treatment

Questions?

Dementie-achtige verschijnselen bij de ouder wordende kat. Dr. Matthijs Schilder

Onderzoeker, Departement Dier in Wetenschap en Maatschappij , Faculteit Diergeneeskunde:

Dementie-achtige verschijnselen bij de kat: oorzaken, diagnose en bestrijding

Dr M.B.H. Schilder
Dept. Dier in Wetenschap & Maatschappij,
Faculteit Diergeneeskunde
Universiteit Utrecht

Cognitieve dysfunctie bij de kat

- Vaker voorkomend dan bij de hond?
- 43% van 152 katten > 11 j verschijnselen
- Deels medisch, maar 33% niet medisch verklaarbaar
- 28% van de katten tussen 11 en 15 j
- 38% van de katten ouder dan 15 j aangetast

(cf Moffat, 2001)

Oorzaken voor dementie-achtige verschijnselen (humaan)

- Acetylcholine dysfunctie
- Arthritis: vatproblemen -veranderde calciumhuishouding
- Veranderde energiehuishouding: verminderde glucosestofwisseling
- Vrije radikalen leiden tot schade→
- Amyloid-cascade hypothese
- Afname van oestrogeen
- Vorming van lewy bodies
- ….

Verschillende vormen van dementie

- Alzheimer
- Parkinson-gerelateerd
- Lewy body dementie
- Vasculaire dementie
- Fronto-temporale dementie
- korsakov-dementie
- Creutzfeldt-Jacob
- ….

Andere oorzaken voor gedrags-veranderingen bij de oudere kat (cf Gunn-Moore 2008)

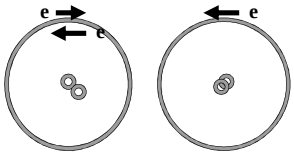
- Hersentumor
- Hersenbloedinkjes, arteriosclerose
- Schildklierdysfunctie (hyperthyroidie)
- Bloedtoevoer naar hersenen verminderd door bv
  - Hartprobleem,Bloedarmoede, Stollingsdefecten, Hoge bloeddruk
- Diabetes
- Chronische nier- of leverziekten
- Infectieziekten (ook in CZS) , pijn, zintuigfalen

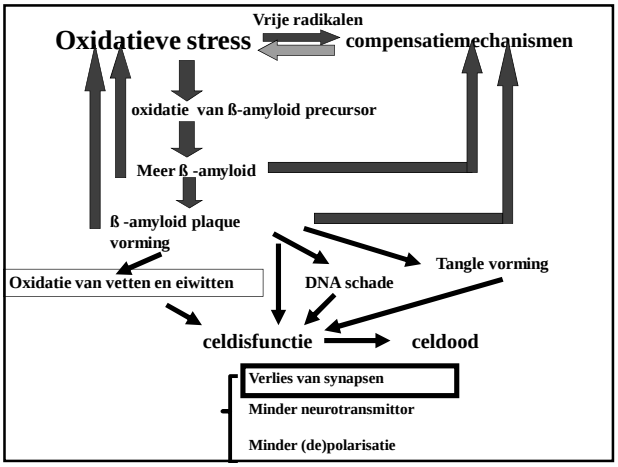
Uitingen van dementie bij de mens

Verlies van hypothetisch, abstract denken
Geen inzicht in ziekte
Egocentrisme
Verlies van zelfbeoordeling / zelfervaring
Motorische en sensorische afasie
Verlies van zindelijkheid
Verlies van herkenning van bekenden en plaatsen
Verlies van reversibel / deductief denken
Verlies van lange termijn perspectief
Verlies van object permanentie
Geheugenproblemen
.....

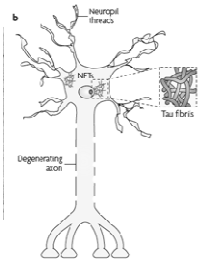
Vrije radikalen

- Atoom met ongepaard(e) electron(en)
- Verbindt zich snel met andere moleculen
- Oxideren andere moleculen
- Leidt tot structuur- en functieveranderingen

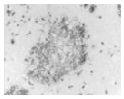


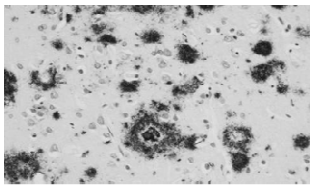


Vorming Tau eiwitten in cel

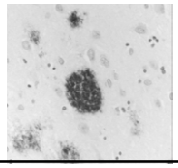


Beta amyloid stapeling



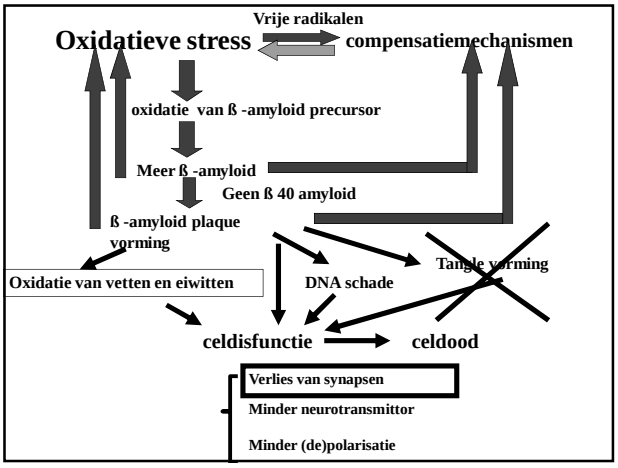


Niet bij hond en kat →

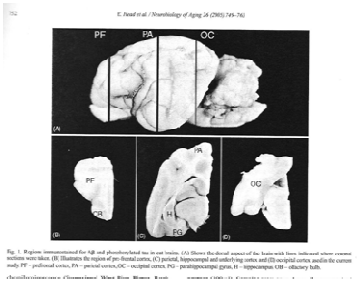


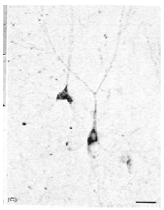
Ook bij de kat…

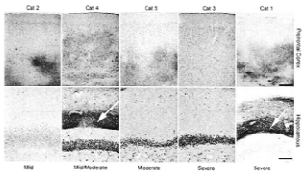
- Beta amyloid stapeling
- Tau afzettingen, maar wel verschillen met die bij de mens. (ander vorm van tau??)
  - Post-mortum onderzoek aan 4 katten >16 jaar met dementie-achtige verschijnselen (Head et al, 2005)



Schade in hersenen van kat cf Head et a 2005







Waarin lijkt de kat op de mens

- geheugenproblemen
- ~~Verlies van hypothetisch, abstract, deductief denke~~n
- ~~Geen inzicht in eigen ziekte~~
- ~~Egocentrisme~~
- Verlies van ~~zelfbeoordeling~~ / zelfervaring ???
- ~~Motorische en sensorische afasie~~
- apraxie
- Verlies van remmingen: zindelijkheid ↓ agressie ↑ e.a.
- Verlies van herkenning van bekenden en plaatsen
- Desorientatie in tijd en ruimte: o.a. zwerven
- ~~Verlies van lange termijn perspectief~~
- Verlies van object permanentie

Waarin lijkt de kat op de mens

- Verstoring van dag-nacht ritmiek
- Verlies van idee van ruimte en volume ???
- Veranderingen in eetgedrag
- Verminderd bewustzijn
- Verminderd initiatief
- agitatie
- onrust

Diagnostiek: we vragen naar:

- **Depressief, passief gedrag**
- **Door te nauwe ruimte willen lopen?**
- **Doelloos gedrag (doelloos lopen)**
- **Ontremd gedrag: actieve incontinentie, agressiviteit, hyperactiviteit, nachtelijke activiteit, veelal met veelvuldig en langdurig miauwen**
- **veranderd sociaal gedrag:**
  - **minder (intensieve)interacties**
  - **zich terugtrekken**
  - **Bedelen maar niet eten als voer wordt aangeboden en daarna weer bedelen** (Gunn-Moore, 2007)

Diagnostiek: we vragen naar:

- **Desoriëntatie in tijd en plaats:**
- **Eetlust: minder makkelijk eten**
- **Verminderd bewustzijn: niet reageren op geroepen worden / prikkels**
- **slechte herkenning van familieleden / maatje**
- **Reacties op veranderingen in omgeving (coping)**

- **Uitsluiten van gezondheidsaspecten**

Behandelingsmogelijkheden bij de kat 1: medicaties

- **Selgian © (=Selegeline)**
  Geen onderzoek bij de kat
- **Vitofyllin**© (= propentofylline) bloedvatverwijderaar: : selectieve adenosineremmer , zou cognitieve functies verbeteren bij de hond (Kapl & Rudolphi (1998);
  geen onderzoek bij kat
- **Fluoxetine / paroxetine**

Behandelingsmogelijkheden bij de kat 1: medicaties

- **Valium of**
- **Alprazolam**
- **Pexion® (imepitione) 1 case studie;** Dubré 2015))
- **= symptoombestrijders**

Behandelingsmogelijkheden bij de kat 2:voedingssupplementen

- **Aktivait** (1 studie: Heath et al,
  - L-carnitine
  - Vitamine C
  - N-acetylsysteine
  - Alpha lipoic acid
  - Vitamine E
  - Acetyl l-carnitine
  - Co-enzym Q10
  - fosfotidylserine
  - Essentiele vetzuren DHA & EPA

Behandelingsmogelijkheden bij de kat 2: voedingssupplementen:

- **Cholodin**
  - Choline
  - Fosfatidycholine
  - Inositol
  - Taurine
  - Zink
  - Diverse vitamine B
  - Methionine
  - EPA en DHA

Behandelingsmogelijkheden bij de kat 3 omgevingsfactoren

- Kat actief houden
- Rijke omgeving (voerspeeltjes)
- Binnen vaste structuur
- Sociale interacties met personen/maatjes

conclusies

- Er zijn dementie-achtige verschijnselen bij de kat
- Hoe ouder; hoe meer schade
- Hersenschade niet gecorreleerd met gedragsveranderingen
- Medicaties ervoor zijn onvoldoende onderzocht
- Voedingssupplementen aanwezig; werkzaamheid nauwelijks onderzocht
- Beste aanpak (voorlopig): verrijking + voedingssupplement

Arthrose bij de kat

Dr. Ronald Jan Corbee
Dierenarts, NL en Europees specialist veterinaire diervoeding

Definitie

Osteoarthrose is de afwijkende reparatie en de eventuele afbraak van gewrichtskraakbeen in associatie met veranderingen in het metabolisme van het subchondrale bot, peri-articulaire osteofyten formatie en een variabele mate van synoviaal membraan ontsteking

Innes 2012

Prevalentie

The Veterinary Journal
journal homepage: www.elsevier.com/locate/tvj

Cross-sectional study of the prevalence and clinical features of osteoarthritis in 100 cats

100 katten >6 jaar geröntgend

>6 jaar 61% arthrose
>14 jaar 82% arthrose

Schouder, elleboog, heup en tarsus

Geen associatie met overgewicht in deze studie

Etiologie

Primaire (idiopathische) OA
Verminderde kwaliteit gewrichtskraakbeen
Aggrecan (afmeting/uniformiteit/functie ↓)→ minder water vasthouden → verminderde weerstand tegen compressie
Verminderde mitotische activiteit
Verminderde reactie op anabole stimuli en groeifactoren
Ophoping versuikeringseindproducten in type II collageen

-> Gevolg: grotere kans op OA bij oudere dieren

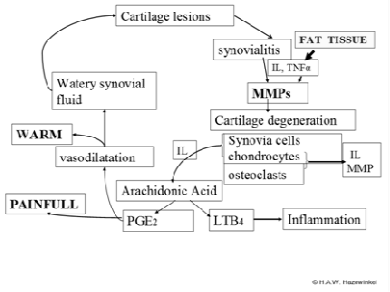
Etiologie

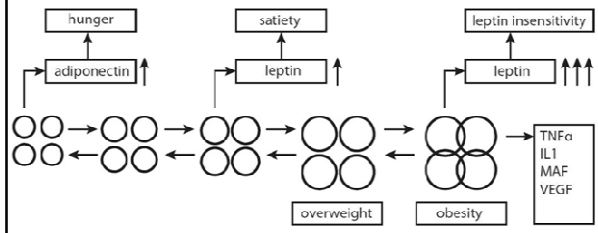
Secundaire OA
Genetische aanleg voor onderliggende aandoening
- HD: Maine Coon, Pers, Siamees
- Patella luxatie: Abbesijn, Devon Rex
- Genetische kraakbeenafwijking: Scottish fold

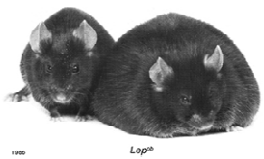
Trauma
Obesitas
Acromegalie
Infectie, immuungemedieerd
Hypervitaminose A
Osteochondromatosis: Burmees
Mucopolysaccharidose

Etiologie

Overgewicht/obesitas
Verhoogde belasting van gewricht
Veranderde gewrichtsaansluiting en dus focale overbelasting
Systemische subklinische pro-inflammatoire status adipokines TNF, IL-6, leptine resulterend in verhoogde expressie van kraakbeenafbrekende enzymen (matrix-metalloproteinases (MMPs))

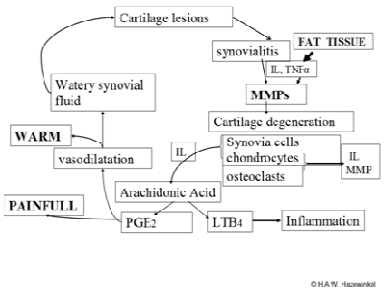




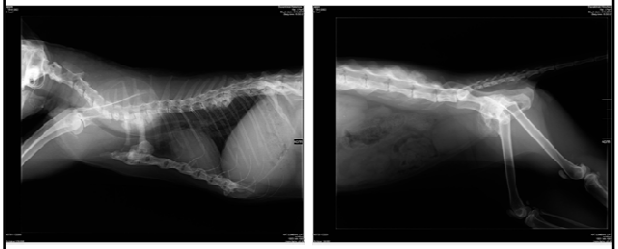


Extreme Obesity Due to Impaired Leptin Signaling in Mice Does Not Cause Knee Osteoarthritis

Timothy M. Griffin, Janet L. Huebner, Virginia B. Kraus, and Farshid Guilak

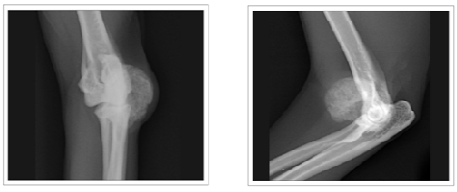


Hypervitaminose A



DKL Kalverbos 2014

Osteochondromatosis



Rosa & Kirberger 2012

Mucopolysaccharidosis

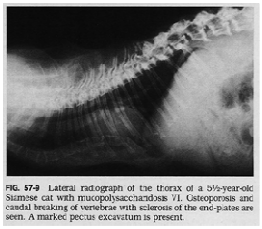
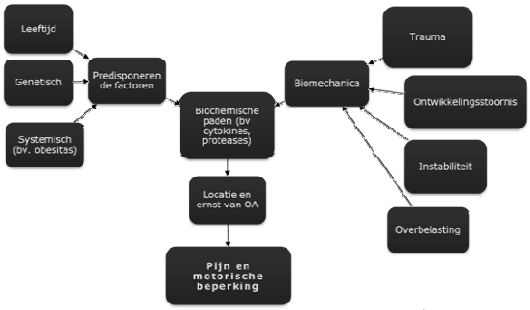


FIG. 57-9 Lateral radiograph of the thorax of a 5½-year-old Siamese cat with mucopolysaccharidosis VI. Osteoporosis and caudal breaking of vertebrae with sclerosis of the end-plates are seen. A marked pectus excavatum is present.

University of Pennsylvania

Etiologie

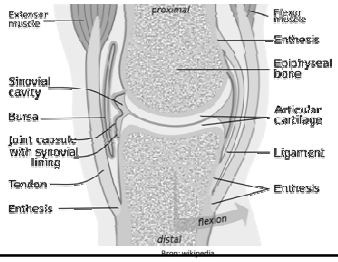


Kranenburg 2015

Anatomie & Fysiologie

Normaal gewricht

Normale belasting



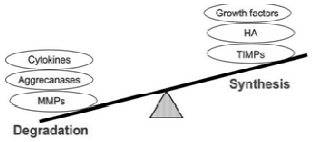
Pathofysiologie

Verstoord evenwicht

Vicieuze cirkel

(Ab)normale belasting

Afname gewrichtskraakbeen



Knee Osteoarthritis

Klinisch beeld

Bemoeilijkte beweging:

Minder springen, lagere hoogtes opzoeken, moeilijker traplopen, stram en soms kreupel lopen, moeilijker door kattenluik gaan, poepen naast de bak

Verminderde activiteit:

Meer rust, slapen

Minder jagen, minder naar buiten

Slapen op andere plaatsen (gemakkelijker toegankelijk)

Minder interactie met eigenaar/andere dieren

Klinisch beeld

Verminderde vachtverzorging:

Minder tijd wordt besteed aan vachtverzorging

Doffe, schilferige vacht

Referred pain: veelvuldig poetsen rondom arthrotische gewrichten

Te lange nagels, slechte verzorging van nagels door verminderde activiteit en minder nagels scherpen

Gedragsverandering:

Minder graag opgetild of aangehaald willen worden

Röntgen en andere beeldvorming

Mate OA op röntgen soms niet gelijk aan klinisch beeld

Osteofyten

Sclerosering

Pijn

Relatie gewrichtspathologie en pijn is niet lineair en niet voorspelbaar

Gewricht zenuwen bevatten Aβ, Aδ en C- fibers

Open zenuweinden zijn in al het gewrichtsweefsel te vinden (incl. ligamenten, kapsel, vetweefsel, meniscus, periost en synoviaalmembraan) maar niet in kraakbeen

Ontstekingsmediatoren (bv. TNF-α, IL-6, bradykinine, PGE-2, PGI-2, serotonine, substantie P, galanine, neuropeptide Y, nociceptie) zorgen ervoor dat C-fibers worden gestimuleerd en maken deze gevoelig voor mechanische stimulatie

Centrale sensibilisatie door COX-enzymen – COX remmer zou via deze weg de verdere ontwikkeling van de OA pathologie kunnen remmen

Therapie

Omgeving:

Zachte ligplaats op een veilige, tochtvrije en warme plaats

Verminderen van hoogtes door opstapjes of loopplanken te gebruiken zodat de kat naar de favoriete plekken op hoogte kan

Kattenluik moet gemakkelijk te openen zijn, eventueel al deels open maken zodat de kat niet hoeft te duwen

Kattenbak in huis met een lage instap

Voer en water moeten op de grond staan of gemakkelijk bereikbaar zijn met opstapjes/loopplank

Neem de tijd voor vachtverzorging en knip te lange nagels regelmatig

Therapie

Outpatient Oral Analgesics in Dogs and Cats Beyond Nonsteroidal Antiinflammatory Drugs: An Evidence-based Approach

Butch Kukanich, DVM, PhD

Pijnmedicatie:

NSAIDs (+bijwerkingen) Meloxicam (0.025-0.05mg/kg PO) (Gowan et al. 2012)

Buprenorphine 0.12mg/kg

Amantidine N-Methyl D-Aspartaat antagonist (3-5mg/kg PO of IV)

Tramadol (1-2mg/kg 2dd PO) onvoorspelbaar effect

Gabapentin (2-10mg/kg 2dd PO) neurogene pijn

Therapie

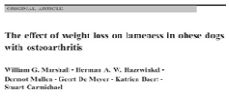
Gewichtsverlies:

Bewezen effectief bij de hond (graad I bewijs), geen studies bij de kat

In aantal prevalentie studies geen correlatie gevonden tussen overgewicht en arthrose bij de kat

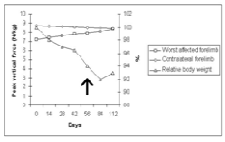
Streven naar gewichtsverlies van 0.5-2% per week

Bij honden al effect bij verlies van 6%


Vet Rec Commun (2008) 34:241–253
DOI 10.1007/s11259-010-9546-7

The effect of weight loss on lameness in obese dogs with osteoarthritis

William G. Marshall · Herman A. W. Hazewinkel · Dermot Mullen · Geert De Meyer · Katrien Baert · Stuart Carmichael



Universiteit Utrecht

Therapie

Nutraceuticals

- Omega-3 vetzuren EPA en DHA: ontstekingsremmend effect
- Glucosamine: onderdeel van kraakbeen
- Chondroïtine: onderdeel van kraakbeen
- Type II collageen: onderdeel van kraakbeen
- Gelatine hydrolysaat: onderdeel van kraakbeen
- Beta-glucanen: ontstekingsremmend effect
- Groenlipmossel: combinatie ETA, glucosamine en chondroïtine

Universiteit Utrecht

Review

J Vet Intern Med 2012;26:448–456

Systematic Review of Efficacy of Nutraceuticals to Alleviate Clinical Signs of Osteoarthritis

J.-M. Vandeweerd, C. Coisnon, P. Clegg, C. Cambier, A. Pierson, F. Hontoir, C. Saegerman, P. Gustin, and S. Buczinski

Background: Various treatments of osteoarthritis (OA) have been described, including use of nutraceuticals.

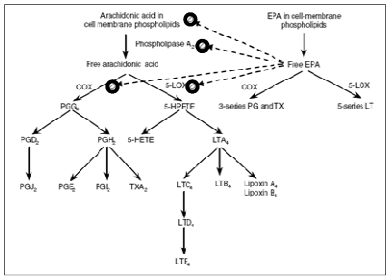
Objectives: To review systematically the literature about the effects of nutraceuticals on clinical signs of pain or abnormal locomotion in horses, dogs, and cats, and to discuss methodological aspects of trials and systematic reviews.

Methods: A systematic search of controlled trials evaluating the impact of nutraceuticals on OA in horses, dogs, and cats was performed, using Medline, CAB Abstracts, and Google Scholar. Scientific evidence was evaluated by means of criteria proposed by the Food and Drug Administration (FDA), and a scoring system adapted from both the CONsolidated Standards of Reporting Trials (CONSORT) statement and recommendations for assessing trials by the Center of Evidence Based Medicine of Oxford.

Results: Twenty-two papers were selected and reviewed, with 5 studies performed in horses, 16 in dogs, and 1 in cats. The strength of evidence was low for all nutraceuticals except for omega-3 fatty acid in dogs. There were limited numbers of rigorous randomized controlled trials and of participants in clinical trials.

Conclusions and Clinical Importance: The evidence of efficacy of nutraceuticals is poor, with the exception of diets supplemented with omega-3 fatty acids in dogs. Greater access to systematic reviews must be part of the objectives of the veterinary science in the future. Their reporting would be improved by internationally agreed-upon criteria for standards and guidelines.

Key words: Dietary supplements; EBM; Evidence; Locomotion.



Synthesis of eicosanoids from arachidonic acid and sites of inhibition by eicosapentaenoic acid

COX,cyclo-oxygenase; EPA, eicosapentaenoic acid; HETE, hydroxyeicosatetraenoic acid; HPETE, hydroperoxyeicosatetraenoic acid; LOX, lipoxygenase; LT, leukotriene; PG, prostaglandin; TX, thromboxane

Calder 2002

Bijwerkingen van EPA en DHA

Review

J Vet Intern Med 2013;27:1427–1436

Potential Adverse Effects of Omega-3 Fatty Acids in Dogs and Cats

C.E. Lenox and J.E. Bauer

Fish oil omega-3 fatty acids, mainly eicosapentaenoic acid and docosahexaenoic acid, are used in the management of several diseases in companion animal medicine, many of which are inflammatory in nature. This review describes metabolic differences among omega-3 fatty acids and outlines potential adverse effects that may occur with their supplementation in dogs and cats with a special focus on omega-3 fatty acids from fish oil. Important potential adverse effects of omega-3 fatty acid supplementation include altered platelet function, gastrointestinal adverse effects, detrimental effects on wound healing, lipid peroxidation, potential for nutrient excess and toxin exposure, weight gain, altered immune function, effects on glycemic control and insulin sensitivity, and nutrient-drug interactions.

Key words: Dietary fat; Dietary supplements; Nutraceuticals; Nutrition.

Therapie: EPA+DHA

Bij de kat zijn er 2 studies naar effecten van EPA+DHA bij arthrose: 1 naar mobility cat diet (Lascelles) met 1.88g EPA+DHA per 1000kcal, en de studie van Corbee et al. met 1.53g EPA and 0.31g DHA per 1000kcal ME

ORIGINAL ARTICLE

The effect of dietary long-chain omega-3 fatty acid supplementation on owner's perception of behaviour and locomotion in cats with naturally occurring osteoarthritis

R. J. Corbee[1], M. M. C. Barnier[2], C. H. A. van de Lest[3] and H. A. W. Hazewinkel[1]

1 Department of Clinical Sciences of Companion Animals, Faculty of Veterinary Medicine, Utrecht University, Utrecht, The Netherlands
2 Applied Biology, High School of Agriculture, 's-Hertogenbosch, the Netherlands, and
3 Department of Biochemistry, Faculty of Veterinary Medicine, Utrecht University, Utrecht, The Netherlands

Universiteit Utrecht

Therapie

Therapeutische diëten

- Bevatten allemaal EPA en DHA
- Bevatten allemaal glucosamine en chondroitine
- Bewezen effectiviteit in meerdere studies
- Effecten zichtbaar na aantal weken

J Vet Intern Med 2010;24:487–495

Evaluation of a Therapeutic Diet for Feline Degenerative Joint Disease

B.D.X. Lascelles, V. DePuy, A. Thomson, B. Hansen, D.J. Marcellin-Little, V. Biourge, and J.E. Bauer

Background: Feline degenerative joint disease (DJD) is common and there are no approved therapies for the alleviation of the associated pain.

Objective: To test a diet high in eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) content and supplemented with green-lipped mussel extract and glucosamine/chondroitin sulfate (test-diet) for its pain-relieving and activity-enhancing effects in cats with painful, mobility-impairing DJD over a 9-week period.

Animals: Forty client-owned cats.

Methods: Randomized, controlled, blinded, parallel group, prospective clinical study. Cats with no detectable systemic disease, and with at least 1 appendicular joint with radiographic evidence of DJD where manipulation elicited an aversive response were included. Cats were randomly allocated to the test-diet or control diet (C-diet). Outcome measures were subjective owner and veterinarian assessments, and objective activity monitoring (accelerometry). Nonparametric statistics were used to evaluate changes within and between groups for both subjective and objective data, and locally weighted scatterplot smoothing regression analysis was used to predict activity changes.

Results: The primary objective outcome measures indicated that activity declined significantly ($P < .001$) in the C-diet group, significantly increased ($P < .001$) in the test-diet group and there was a significant difference between the groups ($P < .001$).

Conclusion and Clinical Importance: A diet high in EPA and DHA and supplemented with green-lipped mussel extract and glucosamine/chondroitin sulfate improved objective measures of mobility. Dietary modulation might be 1 method to use to improve mobility in cats with DJD-associated pain.

Key words: Arthritis; Cat; Mobility; Nutrition.

Royal Canin Mobility Cat, 2010

Table 1. Composition of the diets used in the study.

	Units	C-Diet	Test-Diet
Protein	g/1,000 Kcal	74.96	71.57
Fat	g/1,000 Kcal	37.67	42.23
Crude fiber	g/1,000 Kcal	10.33	7.93
NFE	g/1,000 Kcal	98.07	91.15
Ash	g/1,000 Kcal	14.36	13.37
EPA+DHA	g/1,000 Kcal	0.03	1.88
Total n3 fatty acids	g/1,000 Kcal	0.68	2.97
Total n6 fatty acids	g/1,000 Kcal	7.66	8.03
CS+glucosamine	mg/1,000 Kcal	0.00	250.00
GLM	mg/1,000 Kcal	0.00	74.00
Energy kcal ME/kg as fed	Kcal/kg as fed	3970	4070

Ingredient list (ingredients that were present in test-diet only are presented in italics): Pearled barley, corn, corn gluten meal, rice, wheat gluten, chicken, chicken fat, chicken meal, oat meal, *anchovy oil*, dried egg powder, powdered cellulose, dried beet pulp, ground psyllium seeds, soya bean oil, potassium chloride, calcium, calcium carbonate, fructo-oligo-saccharides, *green-lipped mussel powder*, DL-methionine, brewers yeast extract (source of mannan-oligo-saccharides), potassium citrate, choline chloride, taurine, *glucosamine* hydrochloride, vitamins], Trace Minerals oxide, manganese proteinate, copper (zinc oxide, ferrous, zinc proteinate, copper, manganous proteinate, calcium iodate, sodium selenite], green tea polyphenols, *chondroitin sulfate*, marigold extract, L-carnitine.
CS, chondroitin; GLM, green lipped powder.

Universiteit Utrecht

Therapeutische diëten kat

	Energy	Omega-3	3:6 ratio	EPA+DHA	Glu+CS	Other
Hill's j/d	4040	1,20%	1:3.5	2g	2031mg	Assuming 60:40 EPA:DHA ratio
Royal Canin mobility	3860	NA	NA	7,3g	1000mg	GLM
Specific joint	4018	1,75%	1:1.0	13,1g	2520mg	
	Energy	Omega-3	3:6 ratio	EPA+DHA	Glu+CS	Other
Hill's j/d	970	1,27%	1:3.5	NA	NA	
Specific joint	1224	2,31%	1:2.0	17,8g	3350mg	

Preventie

Geleidelijke groei

Overgewicht voorkomen

Overbelasting voorkomen

Take home message

Onderschatting van probleem, subtiele verschijnselen

Pas de omgeving aan

Belang van pijnstilling: ook veilig op lange termijn

Belang van afvallen

Ondersteuning met supplementen/dieet

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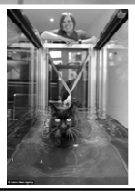
Bedankt voor uw aandacht



Vragen ?

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